Cyanoketene Cycloaddition Reactions

by

Mohammed Muqtar

A Thesis Presented to the

FACULTY OF THE COLLEGE OF GRADUATE STUDIES

KING FAHD UNIVERSITY OF PETROLEUM & MINERALS

DHAHRAN, SAUDI ARABIA

In Partial Fulfillment of the
Requirements for the Degree of

MASTER OF SCIENCE

In

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This thesis, written by

MOHAMMED MUQTAR

under the direction of his thesis committee, and approved by all the members, has been presented to and accepted by the Dean, College of Graduate Studies, in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE IN CHEMISTRY

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In the Name of Allah

the Most Gracious, the Most Merciful

In Memory of

My Parents

ACKNOWLEDGEMENTS

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF SCHEMES

خلاصة البحث

اسم الطالب الكامل : محمد مختـــــار

عنوان الدراســـة : تفاعلات الاضافة الحلقية لمركبات سيانوكيتين

التخصـــــــص : كيميـاء

تاريخ الشهـــادة : يونيه ١٩٩٠ م

لقد تمت دراسة جوانب مختلفه من تفاعلات ٢ + ٢ الحلقيه لثلاثى بيوتيل سيانوكيتين . وقد وجد ان التفاعل الحلقى للاكينات احادية التفرع والمحتويه على ثلاثى بيوتيل ثنائى ميثل اوكسى سليكون مربوطا بذرة كربون غير ألكينية يسير و فق اضافة مكانية وفراغية منتخبة عند إضافتها لثلاثى بيوتيل سيانوكيتين حيث نحصل على الناتج المضاد للدينامي حرارى كمركب وحيد . بيد ان الاضافة لمواد الستايرين ومثوكسي ستايرين لا تسير وفق اضافة منتخبة . بل ان خليطا من المركبات ينتج فى كل حالة وقد أمكن تحويل المركب المضاد للدينامي حرارى الى مركب دينامى حرارى .

لقد وجد ان اضافة ثلاثى بيوتيل سيانوكيتين للاكينات ارا ثنائية الربط والمحتوية على ثلاثى بيوتيل ثنائى ميثل اوكس سيليكون او مجموعة اوكسي بنزيل والمربوطه الى مواقع أليليك او هومو أليليك يعطى خليطا من البيوتانونات الحلقية اضافة الى مركبات غير حلقية ، ناتجة من تفاعلات إين . ورغم ان تفاعل ثلاثى سيانوكيتين مع فينيل أستيلين اعطى بيوتانون حلقى بكفاءة ناتج جيده ، الا ان التفاعل المقابل مع الالكاينات الطرفية غير العطرية مثل : ١ ـ اوكتاين او سايليل ايثر لبروبارجل الكحول ادى الى مركبات حلقية ذات ناتج قليل جدا .

اما تفاعلات ثلاثى بيوتانون سيانوكيتين مع النايترونات الحلقية فقد أدى الى خليط من المركبات المعقدة .

وقد تمت دراسة الثبات الحرارى لمجموعة من حلقات البيوتانونات فى مذيبات مختلفة ودرجات حراره مختلفة . وقد وجد بشكل عام ان حلقات البيوتانونات ذات ٣ر٣ ثنائية الربط أسرع فى التحول الحلقى من حلقات البيوتانونات ذات ٣ احادية الربط . وقد وجد بشكل عام ان ثابت معدل سرعة التفاعل لهذه التحولات الحلقية لايعتمد على نوع المذيبات المستخدمة .

ويبدو ان ميكانيكية التفاعل لهذه الاضافات الحلقية او التحولات الحلقية المعاكسه لايخضع لميكانيكية تفاعل محدده ومعروفه ولكن اعتمادا على طبيعة المادة المتفاعلة مع الكيتين ، فان ميكانيكية التفاعل تتذبذب من خطوة واحدة وتغيرات تحدث فى نفس اللحظـــة مرورا بالخطوه الواحده ـ وتغيرات تحدث فى لحظـــات متباينة الى ميكانيكية التفاعل متعـــدد الخطـــوات والمحتوى على مركب وسيـــط (زفيترأيون) .

درجـــــة الماجستير فى الفلسفـــة

جامعـــة الملك فهـــد للبترول والمعادن

الظهران ـ المملكه العربيه السعودية

التاريخ : يونيـــــــه ١٩٩٠م

THESIS ABSTRACT

NAME OF STUDENTS	:	MOHAMMAD MUQTAR
TITLE OF STUDY	:	CYANOKETENE CYCLOADDITION REACTIONS
MAJOR FIELD	:	CHEMISTRY
DATE OF DEGREE	:	JUNE, 1990

Several aspects of [2+2] cycloaddition reactions of tert-butylcyanoketene (TBCK) with different ketenophiles have been studied. Cycoaddition of mono substituted alkenes having tert-butyldimethylsiloxy group attached to non-alkenic carbon has been found to undergo regio- and stereo-selective addition to TBCK to give contrathermodynamic product as the sole adduct. However addition to styrene and p-methoxy styrene was found to be non-selective and a mixture of adducts were formed in each case. A way has been found to convert the contrathermodynamic adduct to the thermodynamic product.

Addition reaction of TBCK with 1,1-disubstituted alkenes having t-butyldimethylsiloxy, or benzyloxy group attached to allylic or homoallylic positions afforded a mixture of cyclobutanones in addition to acyclic product arising out of ene reaction.

Even though the addition reaction of TBCK with phenylacetylene gave cyclobutanone in good yield, the corresponding reaction with aliphatic terminal alkynes, such as, 1-hexyne, 1-octyne or silyl ether of proporgyl alcohol afforded the cycloadduct in very low yield.

Cycloaddition of TBCK with cyclic nitrones afforded a complicated mixture of intractable products.

The stability of several cyclobutanones in different solvents and temperature are studied. In general 3,3- disubstituted cyclobutanones are found to undergo cycloreversion faster than the 3-substituted cyclobutanones.

The rate constants for the cycloreversion of several cyclobutanones were found to be more or less solvent independent.

The mechanism of the cyloaddition or the cycloreversion does not seem to have a unified mechanism. Depending on the nature of the ketenophiles, the mechanism seems to vary from concerted-synchronous to concerted asynchronous or to stepwise mechanism involving zwitterion intermediate.

MASTER OF SCIENCE DEGREE

KING FAHD UNIVERSITY OF PETROLEUM & MINERALS

DHARAN, SAUDI ARABIA

DATE: JUNE, 1990

1. INTRODUCTION

Cycloaddtion reactions of t-butylcyanoketene (TBCK) to the various alkenes is described in this thesis. The main objective of our work is to investigate further the mechanisms of [2+2] cycloaddition of TBCK with a variety of functionalized ketenophiles. TBCK addition to nitrones having β−hydrogen has also been studied briefly.

t-Butylcyanoketene is an electron deficient cumulene, synthesised for the first time by Moore, H. W., in 1970.[1] TBCK is suitable for [2+2] cycloaddition under a variety of experimental conditions. It is thermally stable to self condensation when kept in solution, reactive towards a wide range of unsaturated substrates, unsymmetrical in nature to study the stereochmistry of resulting cyclobutanones, and a starting material that can be used to prepare a variety of carbocyclic and heterocyclic compounds. These experimental advantages made TBCK an ideal reagent for the investigation of the [2+2] cycloaddition reactions.

A great deal of work concerning its addition to many unsaturated substrates has appeared in a review by Moore and Gheorghiu.[2] The cycloaddition of these ketenophiles with few exceptions believed to occur through zwitterionic intermediate.

A detail survey of ketene-ketenophile cycloaddtion reactions is made in the " HISTORICAL" section. The outcome of results are given in

"RESULTS AND DISCUSSION." The detailed experimental work is described in "EXPERIMENTAL" section. The bibliography is listed in "REFERENCES" section.

2. HISTORICAL

[2+2] - Cycloaddition reactions of ketene with various ketenophiles have generated a lot of interst and has become the issue for a number of reviews.[2,3,4]

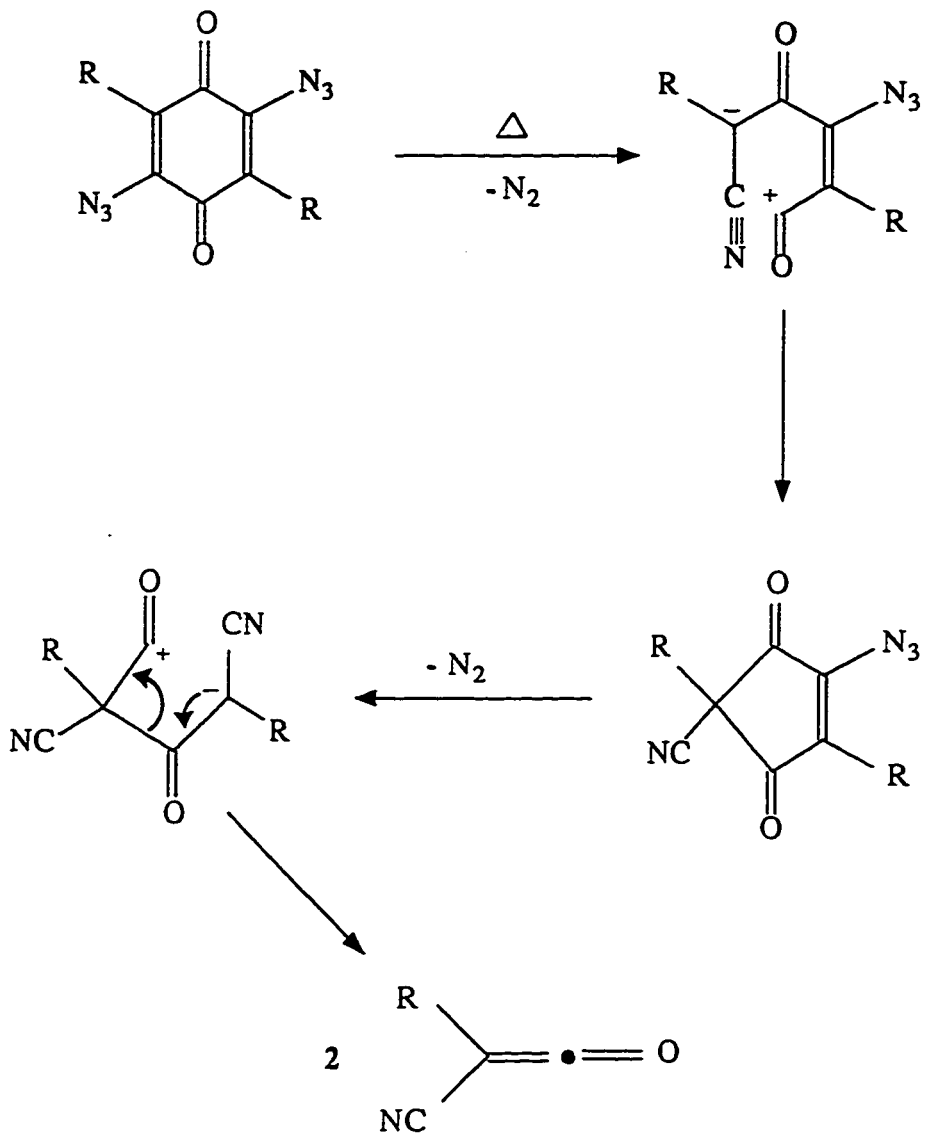
Ketenes in general undergo reactions with a variety of ketenophiles (alkenes, alkynes, allenes, ketenes, imidates, imines, aldehydes, isonitriles, amine oxides, azirines, sulphurdi-imides, etc).[2,3]

Cyanoketenes are the most extensively used, readily available class of electron defficient cumulenes. These are prepared from thermolysis of appropriately substituted vinly azides.[4] The general route to various cyanoketenes is outlined in scheme 1.

Monosubstituted, disubstituted and trisubstituted alkenes react with TBCK to give cyclobutanones in [2+2] cycloaddition reactions.

Among monosubstituted alkenes, cycloaddition reactions of TBCK with styrene has been studied extensively.[5,6,7] The sole reaction product is the cyclobutanone having cis stereochemical relationship between the bulky t-butyl group and phenyl substituents. Such a result was best rationalized in terms of concerted $2\pi_a + 2\pi_s$ reaction mode.[8] The mechanism further demands preservation of alkene stereochemistry in cyclobutanone product, such was observed for TBCK addition to Z and E isomers of mono and dideuterated

Scheme 1



R= — $C(Me)_2Et$, — CMe_3 , — $CHMe_2$, —Me, — Ph , — CN

styrene to give preserved stereochmistry in cyclobutanones.

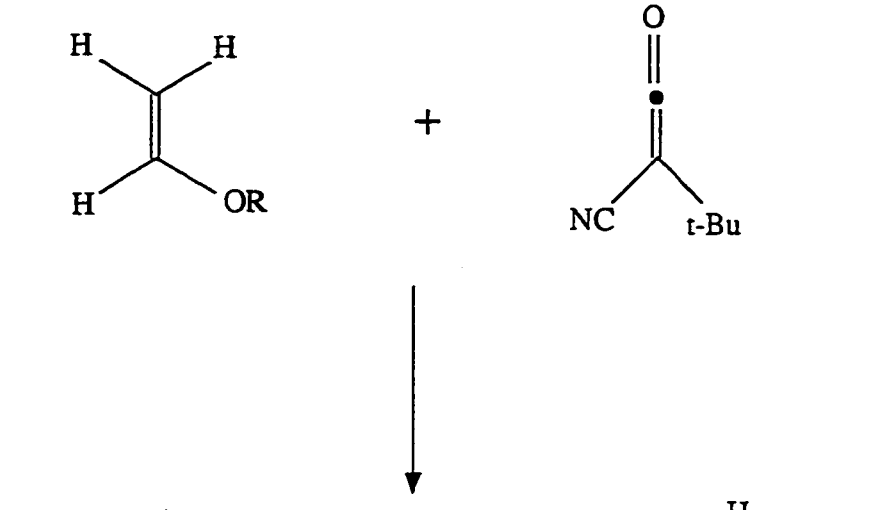
A zwitterionic mechanism is most likely for the cycloaddition of TBCK to electronically rich enol ethers.[9] Ethyl vinly ether and vinly acetate gave the corresponding cyclobutanones 1 - 4 upon treatment with TBCK (scheme 2).

One slight selectivity observed for the formation of contrathermodynamic product 1 and 3 was viewed as arising from the favored sequence indicated in the proposed zwitterion 5, i.e., small group rotating past small proton. Such a process is in consistent with the predictions arising from orbital correspondence analysis in maximum symmetry (OCAMS), which proposes specifically oriented zwitterions or diradicals in [2+2] cycloaddion.[10,11] However, OCAMS theory has been disqualified recently by Al-Husaini and Moore[18,19].

The cycloaddition of ketenes to silyl enol ethers has been investigated extensively by many workers. Dichloroketenes are found to react readily with enol ethers affording regio- and stereo-specific cyclobutanone products in most cases.[12]

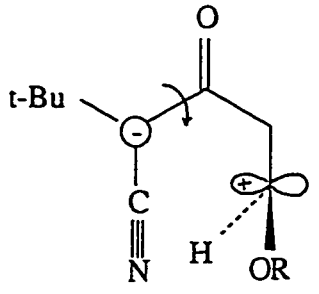
Although the regiochemistry of the cyclobutanone suggests electronic control with the possibility of a dipolar intermediate, the sterochemical results indicate that such species do not have an appreciable life time and thus reaction proceeds via stereospecific concerted cycloaddition. The silyl enol ethers derived from acetophenone and pinacolone afforded only acyclic products with the dichloroketene. Possibly the acyclic products could have

Scheme 2



1. (R=Et)
3. (R=COMe)

2 .. (R= Et)
4. (R= COMe)



resulted from initially formed cyclobutanones followed by ring opening reactions or the cyclobutanone formation was not at all involved, i.e., the dichloroketene simply acylated the silyl ethers.

Cycloaddition of dichloro- and methylchloro-ketene with several conjugated trimethylsilyl enol ethers has been studied[13,14] An intersting reaction of this type was the addition of dichloroketene to the trimethylsilyl ether of 2-cyclopentenone, which gave two products in a 4 : 1 ratio. The major product was a cycloadduct while the minor product was determined to be its acyclic isomer. Although a thermal ring opening is possible, it is unlikely that the minor acyclic product was derived from the cyclic one. At no time was the reaction mixture heated. When the reaction mixture was distilled, there was no evidence of further ring opening and the same ratio of products were obtained as observed in NMR spectrum. It is possible that an acyclation-type mechanism is the source of acyclic product. Alternatively a dipolar intermediate could account for both of the prodcuts. In cycloaddition of dichloroketene to trimethylsilyl ether from 2-cyclohexenone, it was not possible to isolate the cycloadduct, but its presence was evidenced by IR and NMR spectra of the reaction mixture. When the crude reaction product was distilled, partial rearrangement to the acyclic product was observed. Prolonged heating led to the acyclic product.

Raynolds et al.,[15] investigated the reaction of diethylketene and diphenylketene with various silyl enol ethers. The formation of rearranged adduct in addition to the normally expected cycobutanone, was taken as an

indication that the reaction proceeds by an ionic mechanism. Diphenylketene reacted exothermally with t-butyldimethylsilyl enol ether at room temp. to give 6 (Scheme 3). As heating was continued for two hours to complete the reaction, it was found from the NMR analysis that proportion of 7 has increased, and after 24 hours, all 6 has disappeared. The NMR spectra showed that 7 was present, even at very low concentration. It was shown that the changing ratio 6:7 was due to the slow conversion of 6 to 7 at 135° C, which strongly supported a non-concerted cycloaddition.

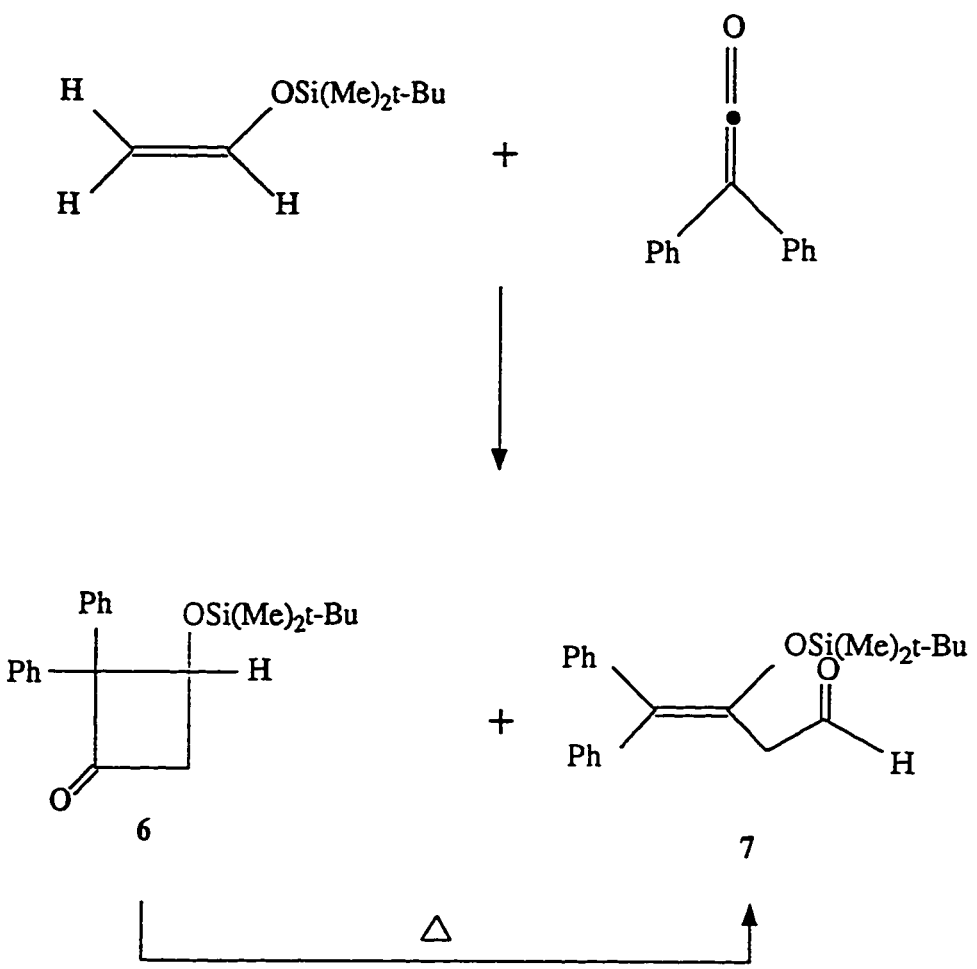
1,2-Disubstituted alkenes react readily to give cyclobutanones. Anticipated cis-relationship between the bulky tertiary group and the substitution at position 3 was observed, indicating the preservation of alkene stereochemistry in the product.[16]

For example, treatment of cis and trans-cyclooctene with TBCK gave, respectively, 8 and 9 (Scheme 4). Cyclohexene has also been observed[17] to form cycloadduct 10 with TBCK.

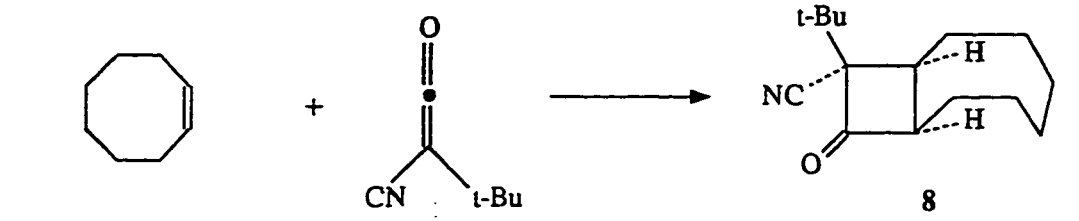
Although stereochemical evidence for 10 is lacking, sterochemical relationship is presumed to follow analogous to 8 and 9 , i.e., t-butyl group cis to adjacent CH_2. Similarly cis-but-2-ene gave cyclobuanone 11 .

A brief report has appeared describing the cycloaddition of TBCK to an acyclic conjugated diene[17]. Treatment of TBCK with trans-trans-2,4-hexadiene resulted in > 80% yield of the cyclobutanone 13 (shchme 5). Cyclobutanone 14 would have been formed exclusively if the cycloaddition

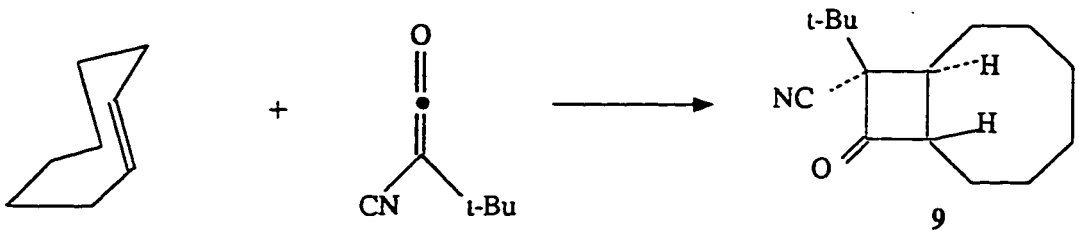
Scheme 3



Scheme 4



8



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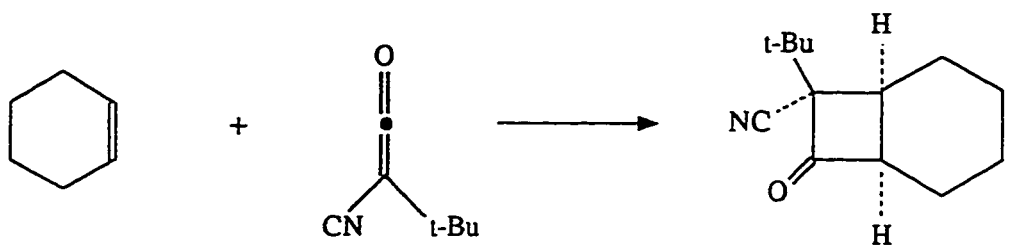

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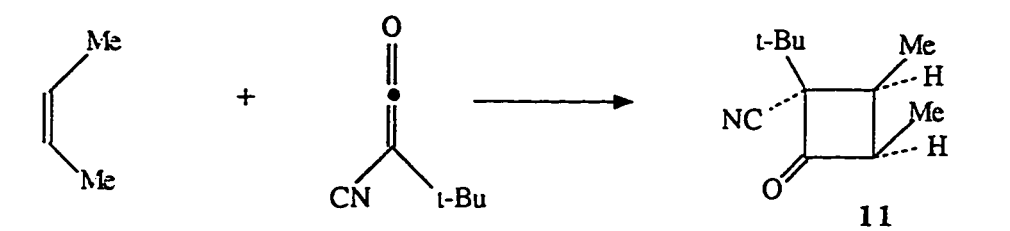


11

were concerted. Thus stepwise mechanism involving a zwitterion 12 may be involved. In a similar study[18] zwitterionic mechanism was proposed for the cycloaddition of TBCK to cic-cis and cis-trans-2,4-hexadiene.

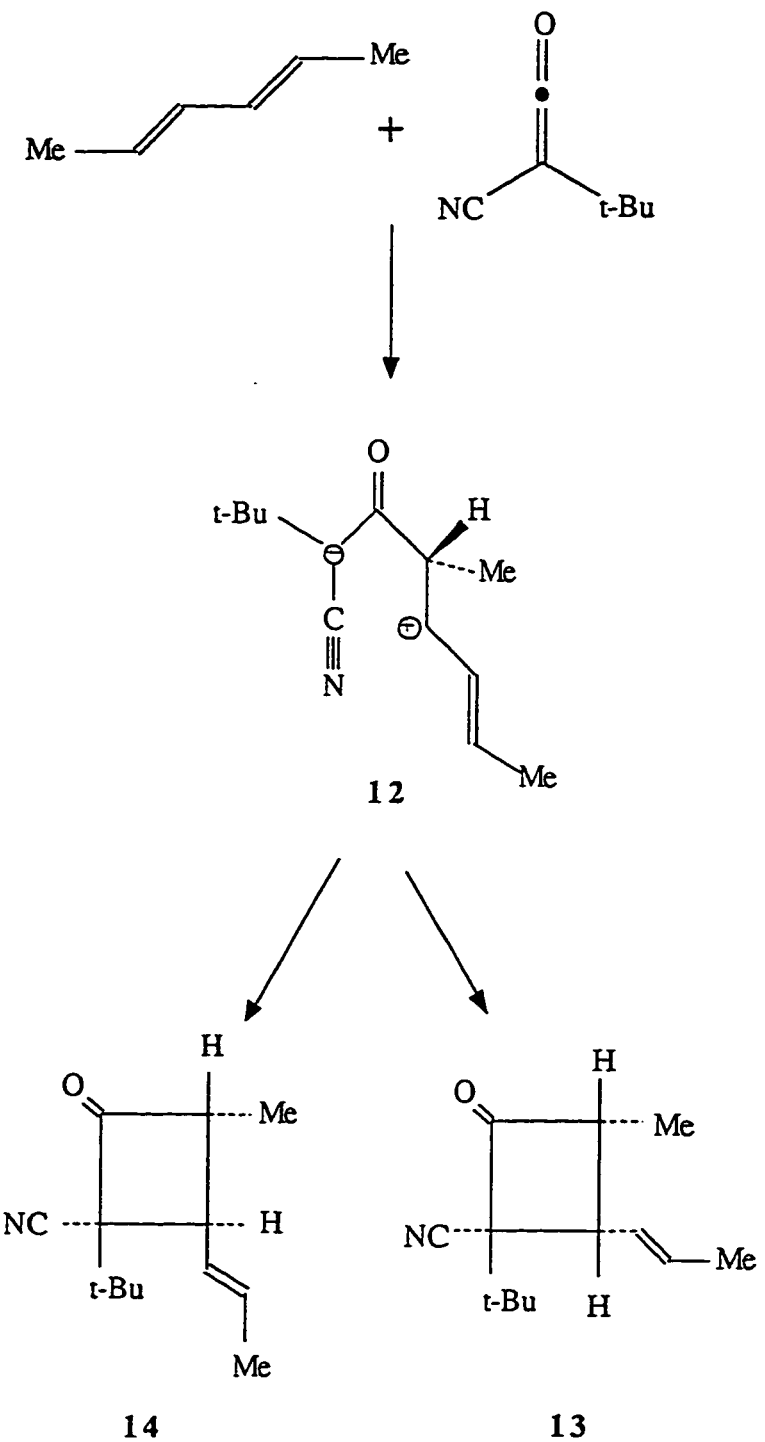
Cycloaddition of various alkyl and silyl enol ethers to cyanoketenes has been extensively studied by Al-Husaini et al[18,19]. The results obtained strongly suggest that zwitterionic mechanism is operating in [2+2] cycloaddtion of TBCK with alkyl and silyl enol ethers. Scheme 6 outlines an example of the above mentioned cyloaddition and the zwitterionic intermediates.

Geminal disubsituted alkenes, e.g., 2-methylpropene, gave[21] cyclobutanone 15 and ene product 16 when treated with TBCK, a result consistent with a concerted $2\pi_a + 2\pi_s$ mechanism of cycloaddtion (scheme 7).

In a recenet study, cycloaddition reactions of enol ethers having electronically and sterically different R group were used to investigate the [2+2] cycloaddition reactions[20] (scheme 8).

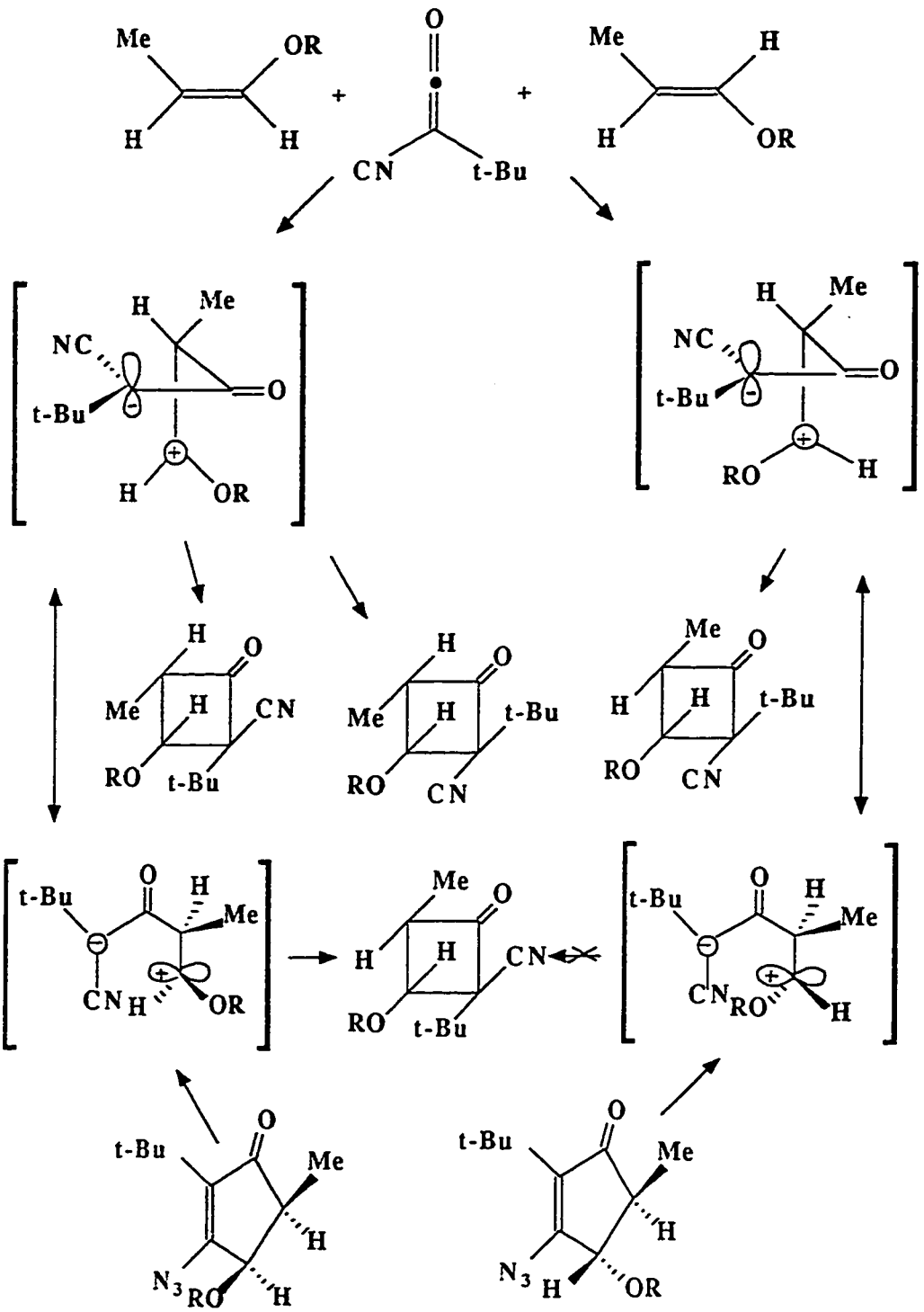
The stability of zwitterion 18 (scheme 9) was determined by the electronic as well as steric factors of R group; if the magnitude of electron donating power of group R is more, then the zwitterion 18 will be more stable. One the other hand increasing the size of the R group will introduce steric interactions with the bulky tertiary group of TBCK. It was shown that the enol ethers described (scheme 8) reacts with TBCK affording only acyclic products (Scheme 10), which was suggested to form by ring opening of an initially formed cyclobutanone species.

Scheme 5



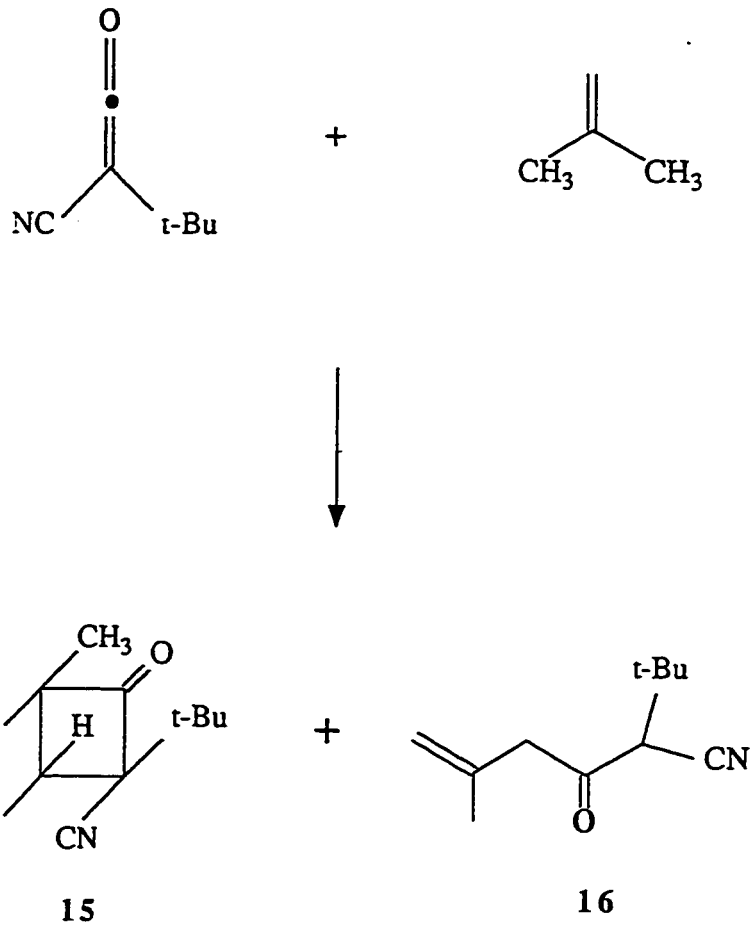
14 **13**

Scheme 6



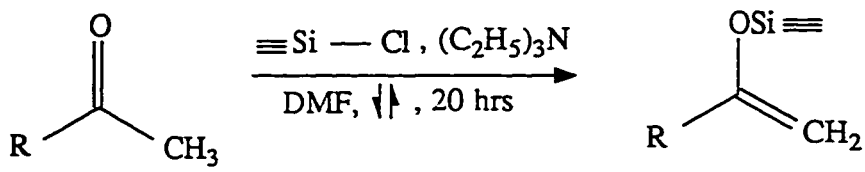
R = $SiMe_3$

Scheme 7



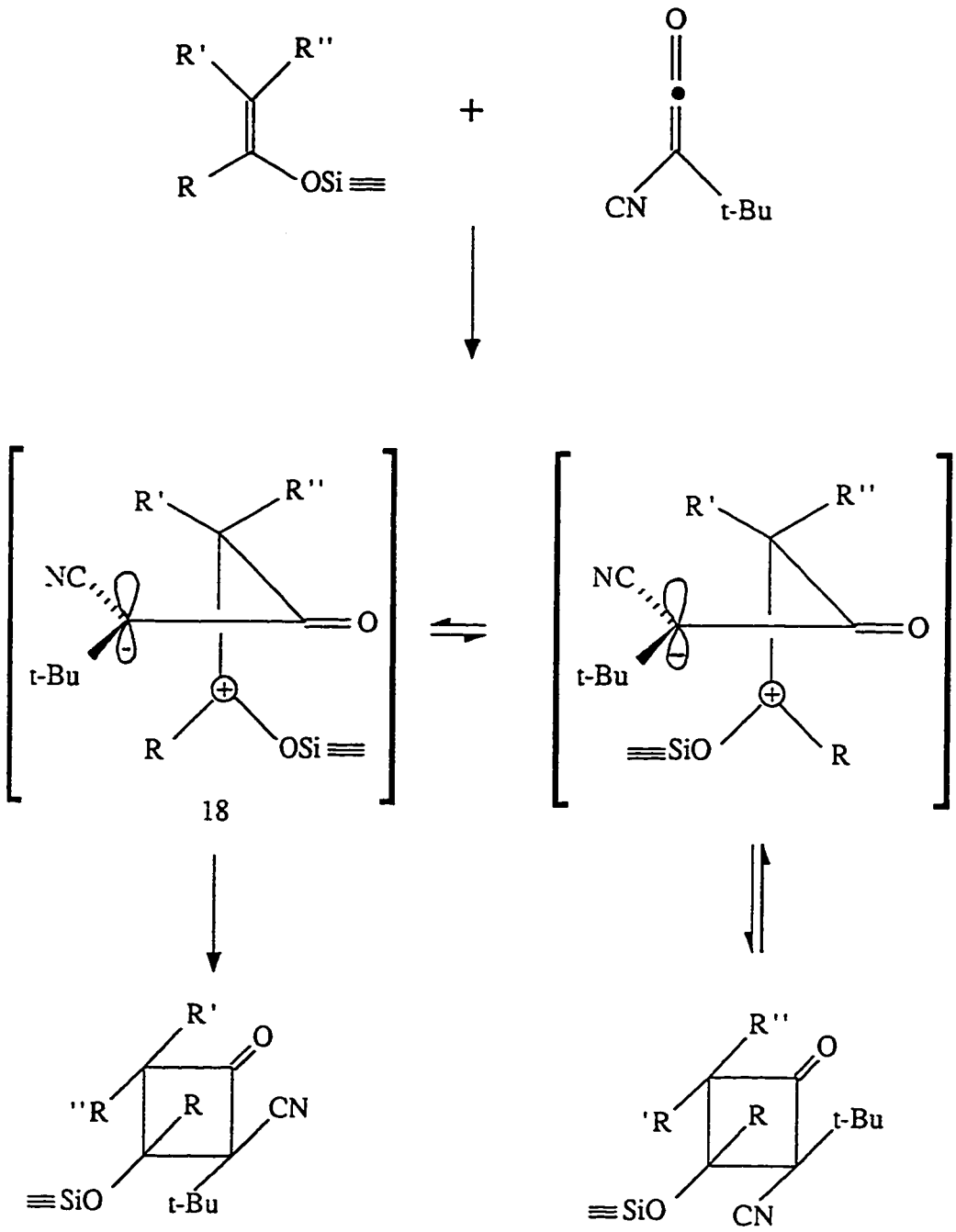
15 **16**

Scheme 8



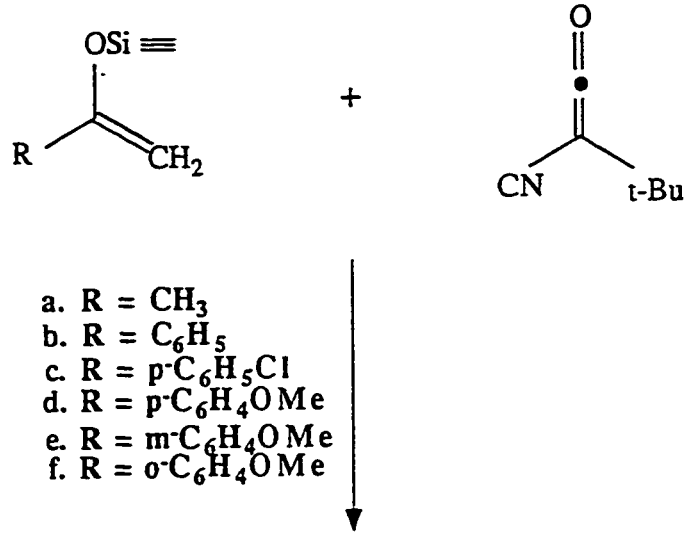
17 a. $R = CH_3$
b. $R = C_6H_6$
c. $R = p\text{-}C_6H_4Cl$
d. $R = p\text{-}C_6H_4OMe$
e. $R = m\text{-}C_6H_4OMe$
f. $R = o\text{-}C_6H_4OMe$

Scheme 9



R'=R''=H

Scheme 10



19. (b,c,d)

20. (a,b,c,d,e,f,)

It was concluded[20] from the above mechanisitic investigation that the reaction of enol ethers (in scheme 8) with TBCK proceeded by ionic mechanism through the zwitterionic intermediate 21 (scheme 11).

Trisubstituted alkene e.g., 2-methyl-but-2-ene, in a cycloaddition with TBCK give only the cyclobutanone 22 (Scheme 12), no ene product found to be formed.[22]

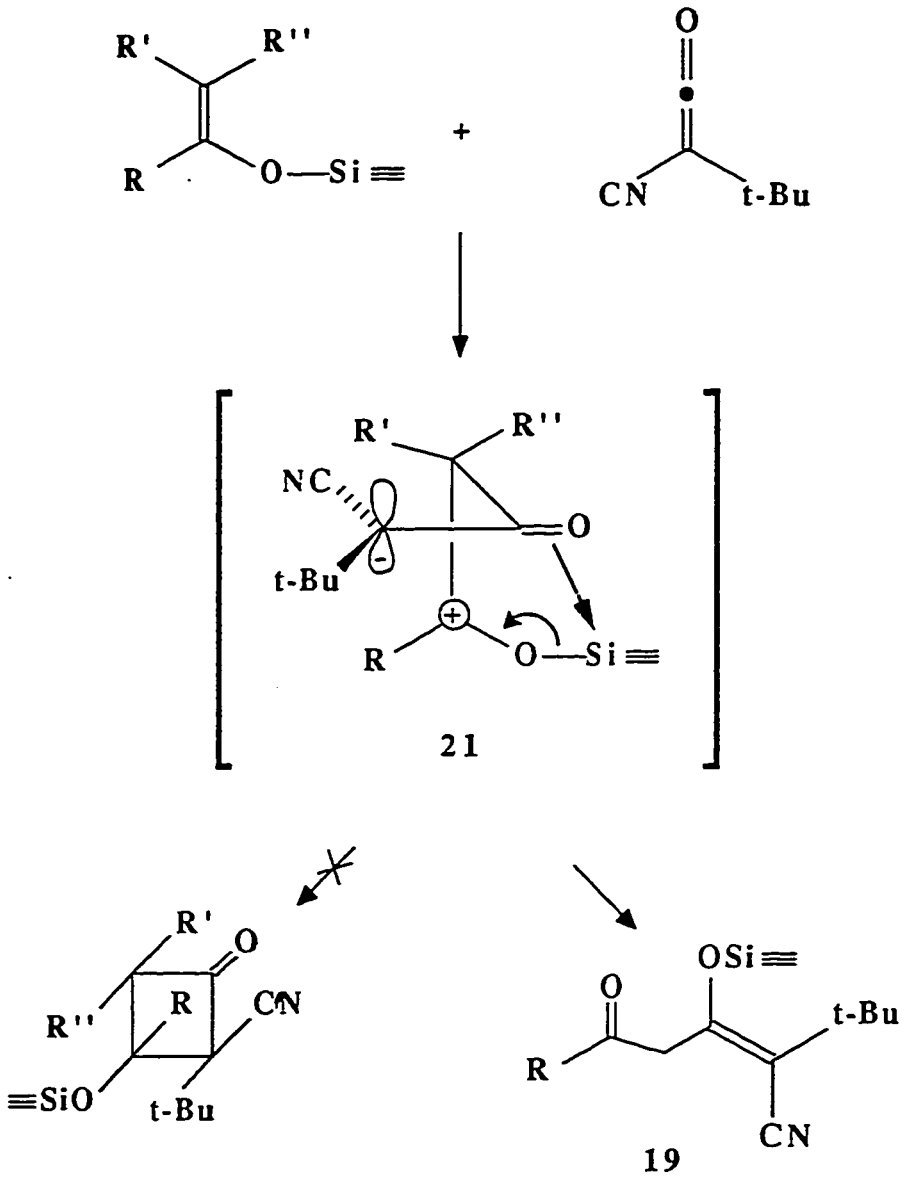
TBCK cycloaddition of strained alkene 1,3,3-trimethyl cyclopropene, has been studied.[24] Apart from regular cyclobutanone, rearranged products were reported to form. A similar preference for rearranged products from these strained alkenes was observed when 1-methyl-cyclopropene was treated with TBCK. No cyclobutanone was formed in this case.[17]

So far there is no example of cycloaddition of tetra substituted alkene to TBCK.

Very few reports have appeared concerning the cycloaddition of cyanoketene to simple alkynes,[25,26] . The ketene used here is TBCK and the product with various alkynes are cyclobutenones. Unsymmetrical alkynes in cycloaddition to TBCK resulted in a single regioisomer, a result consistent with a concerted cycloaddition.

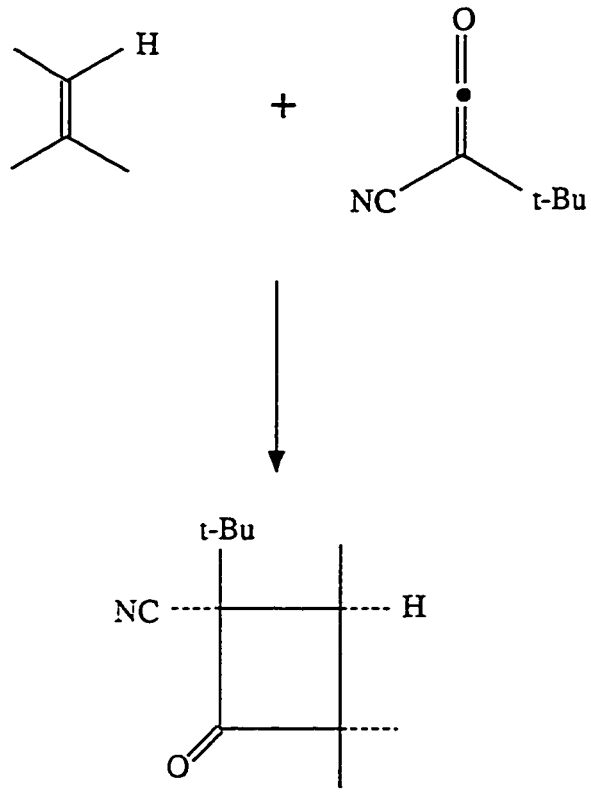
Alkynylcyanoketenes were synthesised and investigated recently.[27] Ketenes shown in scheme 13 are the first known example in which alkyne is directly conjugated to ketene. The ketenes were obtained by refluxing the

Scheme 11



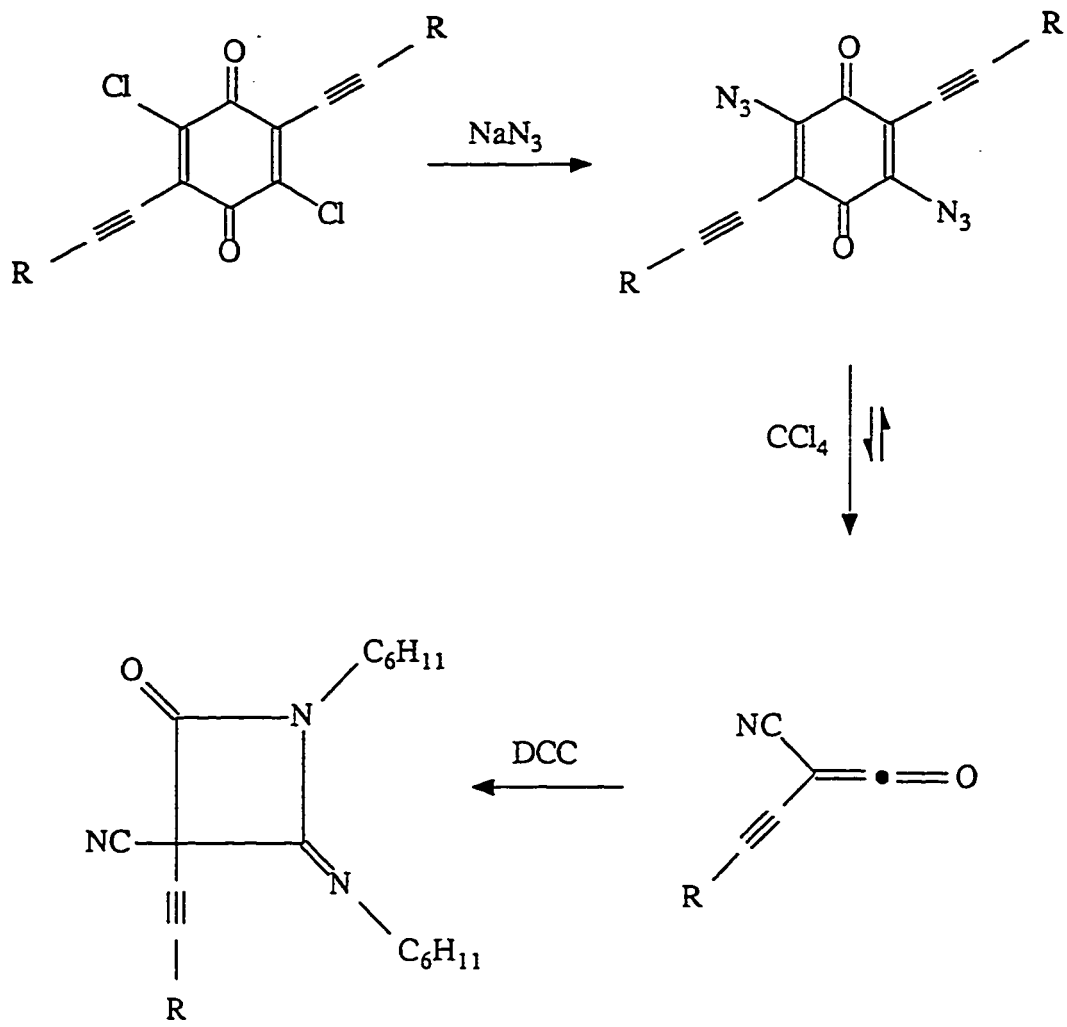
R' = R'' = H

Scheme 12



22

Scheme 13


R
O
Cl
NaN3
N3
CCl4
C6H11
N
DCC
NC
R = — nC4H9, — C6H11, — C6H4 — O CH3, — CH2CH2C6H5,
DCC = C6H11 — N = C = N — C6H11

dizidoquinone precursors in carbontetrachloride. The ketenes were then trapped via their cycloaddition to DCC to give the respective cycloadducts (scheme 13).

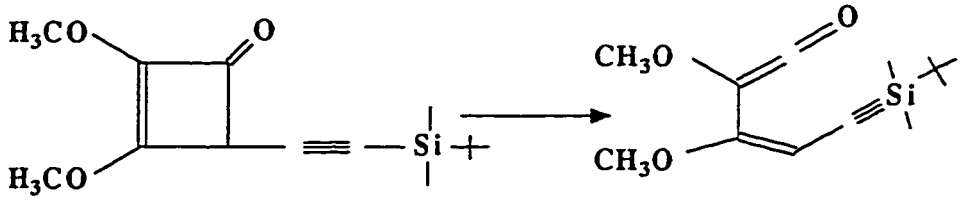
Intramolecular addition of alkyne to ketene has started appearing.[28] One such example is given in scheme 14. Here 25 involves diradical. This diradical undergoes intramolecular hydrogen atom transfer and ultimately gives 26

The first examples of intramolecular [2+2] cycloaddition of ketene to alkenes were reported in 1960s. In early 1980s several groups began systematic exploration of this reaction in the synthesis of complex natural products. Intramolecular [2+2] cycloaddition reactions have been nicely reviewed by Snider,B.B.[29]

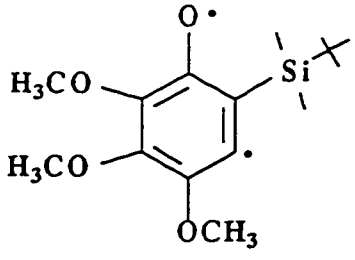
Different types of ketene-alkene cycloadditions to versatile synthetic intermediates are summerized in scheme 15 that goes through ketene intermediate.

In a recent paper[30] the author reported the synthesis of calabar bear alkaloid physovenine. Similarily Corey reported the total synthesis of (±)-β− trans-Bergamotene using intramolecular ketene-alkene cycloaddition for obtaining cyclobutanone ring.[31] It was shown that the reaction proceed asynchronously. In the asynchronous transition state the ketenic carbon can strongly bond to the terminal methylene carbon (electrophilic attack in the Markovnikov's sense) and from this structure the second bond can be smoothly formed.

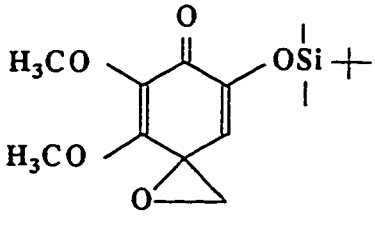
Scheme 14



24

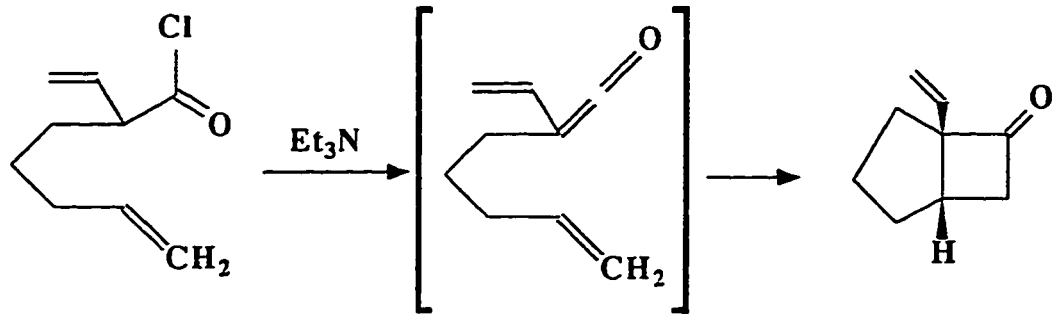


25

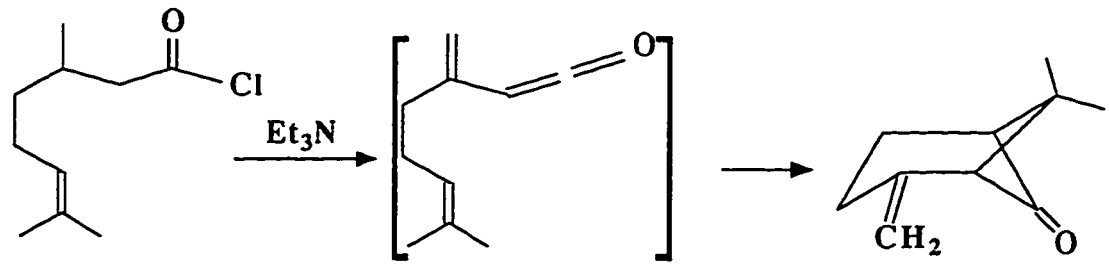


26

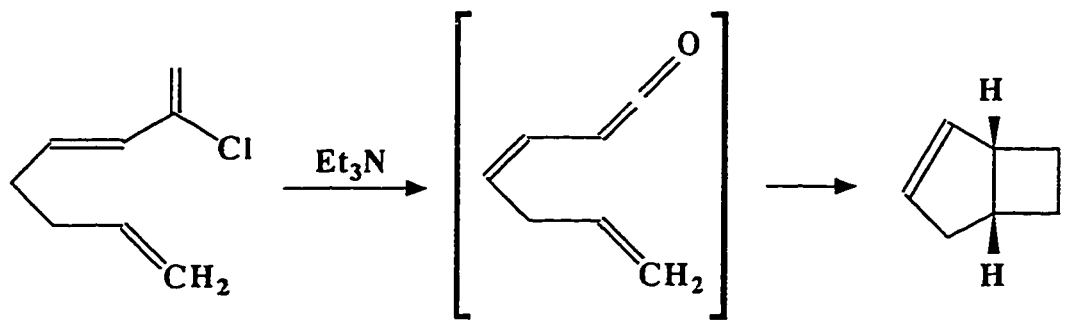
Scheme 15



Type 1 27



Type 2 28



Type 3 29

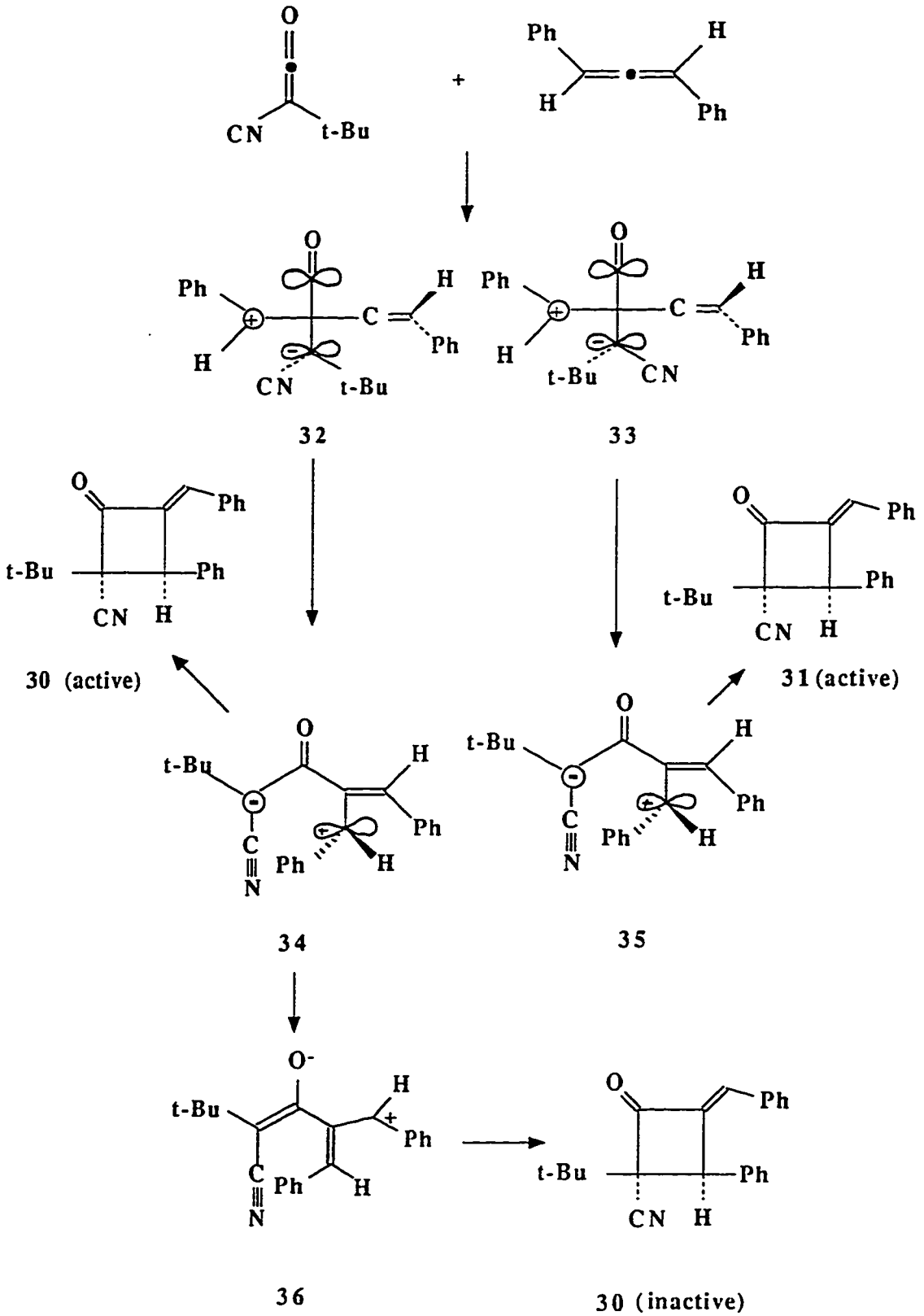
The cycloadditions of TBCK to allenes have been studied in greater depth.[32,33] One such reaction is the cycloaddtion of TBCK to optically enriched 1,3 diphenyl allenes which gave two cyclobutanones 30 and 31 (scheme 16). The mechanism as shown resembles a concerted reaction in that the ketene and the allene components approach one another in orthogonal fashion. However, intial bond formation takes place to give the chiral zwitterion 32 and 33.

Ring closure of these gives, respectively, the optically active products 30 and 31.

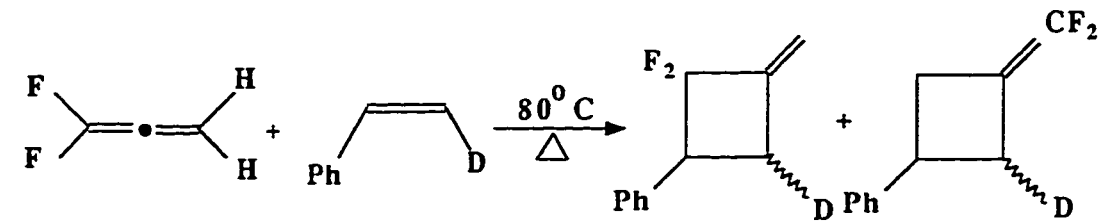
Zwitterions 32 and 33 could assume another chiral conformation 34 and 35 respectively, and these could also undergo ring closure to give 30 and 31. Finally 30 could proceed to the achiral 34 and conrotatory ring closure of this would lead to optically inactive 30.

Dolbier, W.R. Jr., and co-workers proposed[34,35] diradical mechanism for the [2+2] cycloaddition of 1,1-difluoroallene (DFA) and styrene. The relative reactivity factors and the sterochemistry of cycloadducts can be better rationalised by a mechanism involving two kinetically distinguishable diradicals. The products obtained from the cycloaddition of DFA with Z-E-deuterostyrene are also consistent with the hypothesis of diracidcal mechanism. Invovking at least two kinetically distinct intermediates is necessary to account for the observed differences in the degree of retention of configuration in the two products 37 and 38 (scheme 17).

Scheme 16

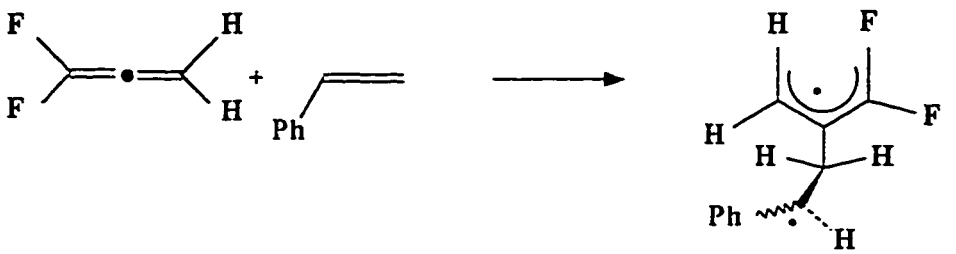

O
CN
t-Bu
+
Ph
H
H
Ph
O
Ph
H
C
H
Ph
CN
t-Bu
32
O
Ph
H
C
H
Ph
t-Bu
CN
33
O
Ph
t-Bu
Ph
CN
H
30 (active)
O
Ph
t-Bu
Ph
CN
H
31 (active)
O
t-Bu
H
Ph
C
N
Ph
H
34
O
t-Bu
H
Ph
C
N
Ph
H
35
O-
t-Bu
H
Ph
C
N
Ph
H
36
O
Ph
t-Bu
Ph
CN
H
30 (inactive)

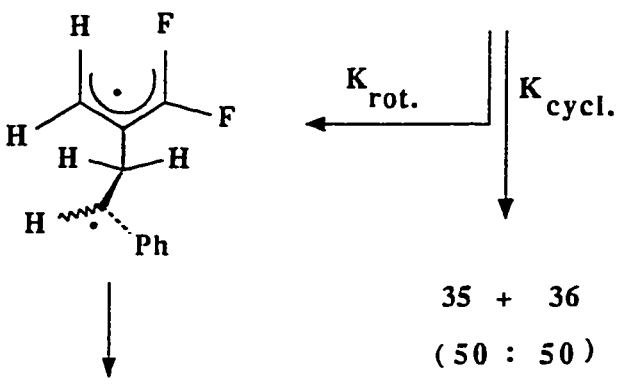
Scheme 17



37 38

58% retention 79% retention





35 + 36

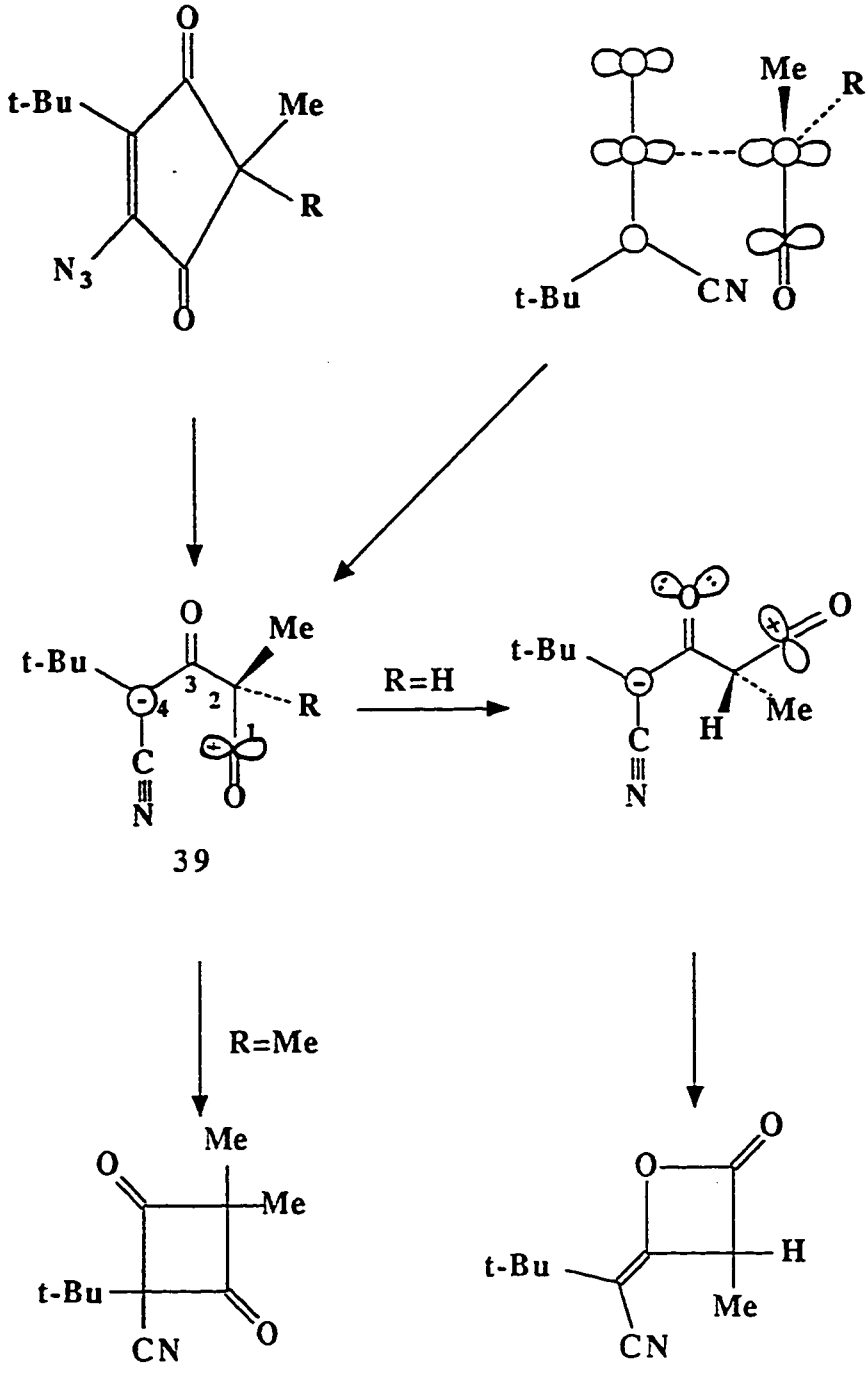
(50 : 50)

mainly 37

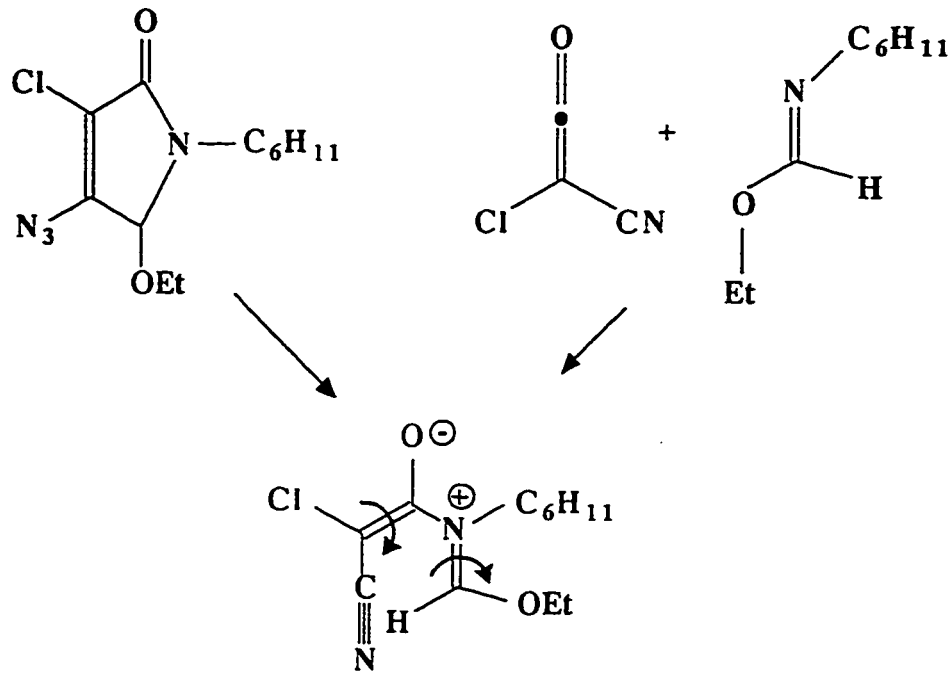
The mechanism of ketene to ketene cycloaddition is ambigous. In the case of cycloaddition of TBCK to aldo and ketoketene it is established that these proceed via a dipolar process.[36] Zwitterion 39 (scheme 18) was independently generated and shown to give the same products as the cycloaddition themselves. Specifically, it was shown that TBCK reacts with ketenes like dimethyl ketene to give cyclobutanones. The most consistent interpretation of these results is that the two ketenes undergo bond formation in a head-to-tail orientation to give the zwitterion represented by 39 (scheme 18).

Extensive studies have appeared concerning the cycloaddition of cyanoketenes to formimides, thioformimidates and imines. Teriarybutyl-, methyl-, chloro-, and iodo-cyanoketens form cycloadducts readily with a variety of acyclic formimidates and thioformimidates to give 3-cyano-2-azetidinones β – lactams[37,38]. Surprisingly the cycloaddition proceed in a stereospecific manner. Sufficient data have now been collected to establish these cycloadditions to be dipolar in character. The most significant mechanistic finding is the independent generation of zwitterion from the thermolysis of 4-azido-2-pyrolinones. For example chlorocyanoketene forms cycloadduct with ethoxy-N-cyclohexyl-formimidates to give 40 (Scheme 19). The same product was formed when 4-azido-3-chloro-1-cyclohexyl-5-ethoxy-3-pyroline-2-one was thermally decomposed in refluxing benzene (scheme 19). In this thermolysis the intermidiacy of zwitterion 41 was established by a series of experiments. It is therefore reasonably assumed that zwitterion 41 is a common intermediate in both the azidopyrolinone decomposition as well as the ketene cycloaddition.

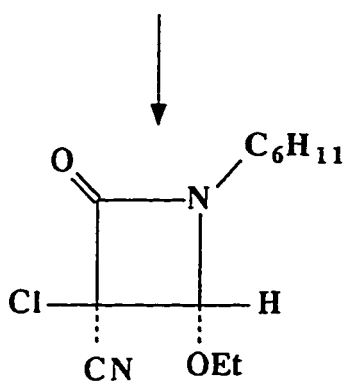
Scheme 18



Scheme 19



41



40

A stepwise pathway that accounts for the observed stereo- and regio-selectivity of the cycloaddition of cyanoketene to cinnamylideneamine was also proposed[40].

Both chloro and bromocyanoketenes undergo cycloaddition with a variety of substituted benzaldehyde[41]. The corresponding β−lactones formed in these reactions suffer stereospecific decorboxylation to give alkenes. It was observed that the relative rates as well as the product yields decreased as the benzaldehyde was substituted with increasingly stronger electron withdrawing groups. Such observations are consistent with a dipolar mechanism in which the ketene funtions as the electrophile and the aldehyde as the nucleophile. This was further substantiated by the independent generation of the zwitterionic intermediate which subsequently gave the same product as the cycloaddition.

Little work has appereard concerning the addition of ketene to isonitriles. Diphenylketene, when treated with benzalisonitrle gave a 2:1 product.[42] Similarily, TBCK has been shown to give 2:1 adduct when treated with isonitrile at ambient temperatures. Here again, zwitterions are reasonable intermediates to these products. Chlorocyanoketene gave the unusual 3:1 adduct, when generated in the presence of excess t-butylisonitrile.

TBCK is also known to react with a variety of 1-azirines to give 2:1 adducts.[43] A 1:1 adduct was observed when TBCK was treated with 2,3-diphenyl-1-azirine. Very limited work has appeared describing the reaction of ketenes with heterocyclic compounds containing two adjacent

heteroatoms.[44] Cycloaddition of ketenes to sulphurdi-imides has recieved little attention, and no reports have previously apperard where cyanoketenes have been utilized. Scuh a study has now been reported[45,46] and the results are unusual in that the observed products are generally different from those reported for less electrophilic ketenes such as phenyl, diphenyl and chlorophenyl ketenes.

3 RESULTS AND DISCUSSION

The main objective of our work was to investigate [2+2] cycloaddition of cyanoketene to various functionalized alkenes and alkynes. Also TBCK cycloaddition to nitrones having β -hydrogen has been studied briefly.

Among alkenes we have used different alkenols having variety of structural features. We have used silyl ethers of monosubstituted alkenols and silyl/benzyl ethers /acetates of 1, 1-disubstituted alkenols.

In monosubstitued alkenols we have choosen t-butyldimethylsilyl ethers of 2-propen-1-ol, 3-buten-1-ol and 4-penten-1-ol. Whereas in 1,1-disubstituted alkenols we have kept one group as methyl and the other group changed upto two carbons, i.e., 2-methyl-2-propen -1-ol and 3-methyl-3-butene-1-ol.

Two different kinds of alkynols were selected for the TBCK addition to alkynes. One is t-butyldimethylsilyl/benzyl ether of 2-propyne-1-ol and the other is t-butyldimethylsily ether of 2-methyl-3-butyne-1-ol.

The purpose of adding functionalized alkene/alkyne to TBCK is firstly to investigate stereo- and regio-chemistry of [2+2] reaction. Secondly the synthetic exploitation of the resulting cyclobutanone/cyclobutenone.

TBCK cycladdition to alkenes such as styrene and p-methoxy styrene and cyclohexene were also done to obtain cyclobutanones for thermal study.

We have studied TBCK cycloaddition to unfunctionalized alkynes for

optimizing the reaction conditions and and for thermal study of resulting cyclobutenones.

Thermal study of a variety of cyclbutanones obtained by TBCK cycloaddition to various alkenes was done. Thermal studies were done in various solvents to understand the mechanism (synchronous/asynchronous/ionic) of [2 + 2] cycloaddition reactions.

3.1 Cycloaddition of TBCK to various silyl/benzyl alkenyl ether(s)/ alkenyl acetate(s)

Cycloaddion of TBCK to t-butyldimethylsilyl-3-butenyl ether (42)

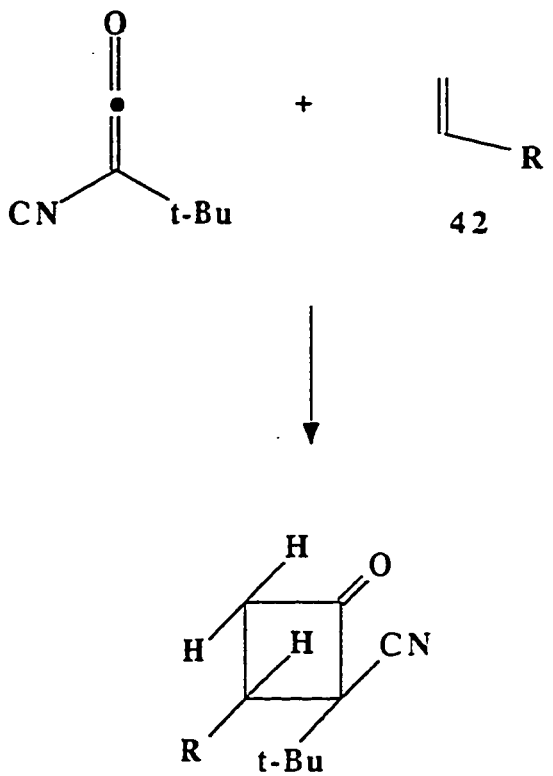
The cycloaddition reaction of TBCK with 42 in refluxing benzene afforded 43 as the sole adduct (scheme 20) in 70% yield. We could not detect the presence of any minor isomer. The CH_2O protons appeared as a triplet at δ 3.70. The protons of C-3 and C-4 carbon appeared as multiplet around δ 3.0.

The sterochemistry as depicted in 43 is based on the assumption that least hindered orthogonal approach of the reactant in $2\pi_s + 2\pi_a$ reaction would place the C-2 t-butyl and C-3 alkyl group in cis orientation. Thus adduct 43 is the contrathermodynamic product.

Cycloaddion of TBCK to t-butyldimethylsilyl-4-pentenyl ether(44)

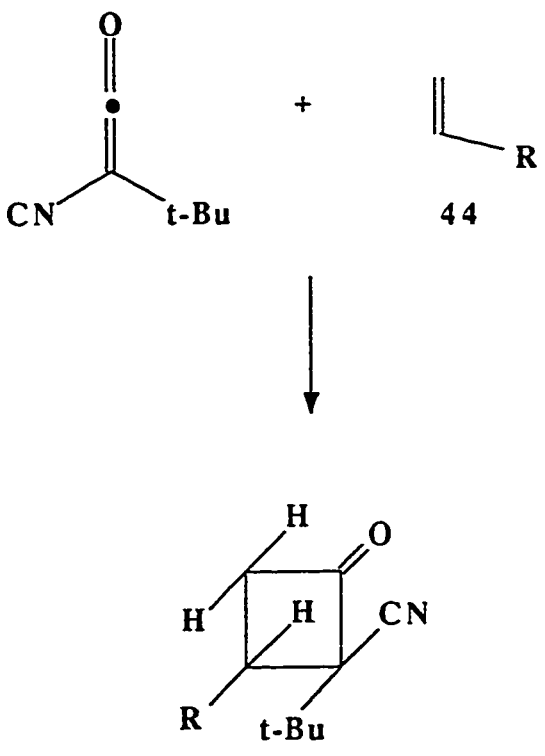
The cycloaddition of TBCK with 44 in refluxing benzene afforded 45 in 65% yield as a colourless crystalline adduct. Careful NMR analysis of the

Scheme 20



43. R = $CH_2CH_2OSi(Me)_2t$-Bu

Scheme 21



45. R = $CH_2CH_2CH_2OSi(Me)_2t\text{-}Bu$

reaction mixture failed to detect the presence of any other minor isomer. The C-2 t-butyl and t-butyl of the silyl group appeard as singlets at 1.22 and 0.90 respectevely. The IR spectra had strong absorption at 1774 Cm^{-1} due to the carbonly group. The CN absorption appeard at 2205 Cm^{-1}.

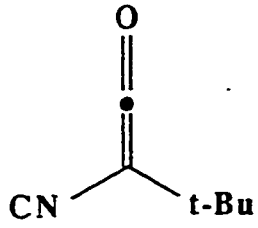
Cycloaddion of TBCK to t-butyldimethylsilyl-
3-methyl-3-butenyl ether (46)

The cycloaddition of TBCK with 46 in refluxing benzene afforded a mixture of several products 47 , 48 , 49 , and 50 (Scheme 22). Due to the proximity in R_f values we were able to separate partially the above products by silica gel column chromatography. Using NMR integraion of the reaction mixture we determined the ratio of 47 , 48 , 49 , and 50, and it was found to be 40 : 33 : 19 : 8, respectively. The major compound was assigned the sterochemistry as depicted in 47 with C-2 t-butyl group cis to bulkier group at C-3. This would be the expected product based on the least hindered orthogonal approach of the addenda.

The C-4 protons of the adduct 47 appeared at δ 2.78 (d, A of an AB, J 17.5 Hz) and 3.38 (d, B of an AB type, J 17.5 Hz). The corresponding protons of the isomer 48 also appeared as a doublet at δ 2.75 (J 18.0 Hz) and 3.14 (J 18.0 Hz).

The formation of the products 49 and 50 are presumably a result of an ene-reaction as depicted in the scheme 23.

Scheme 22



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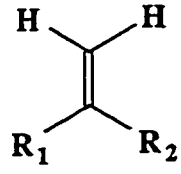
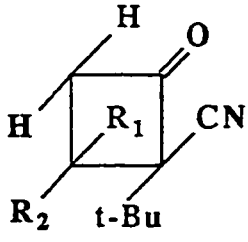


46. $R_1 = CH_3$
$R_2 = CH_2CH_2OSi(Me)_2t\text{-}Bu$



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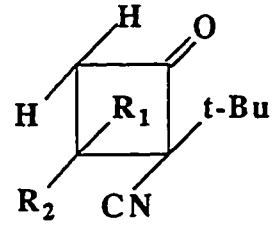
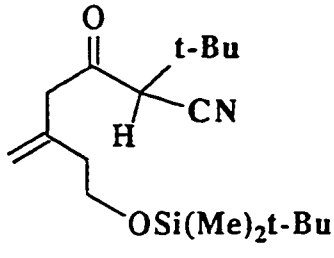
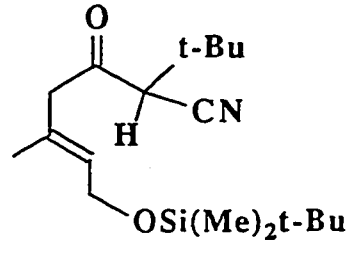


47. $R_1 = CH_3$
$R_2 = CH_2CH_2OSi(Me)_2t\text{-}Bu$

48. $R_1 = CH_3$
$R_2 = CH_2CH_2OSi(Me)_2t\text{-}Bu$



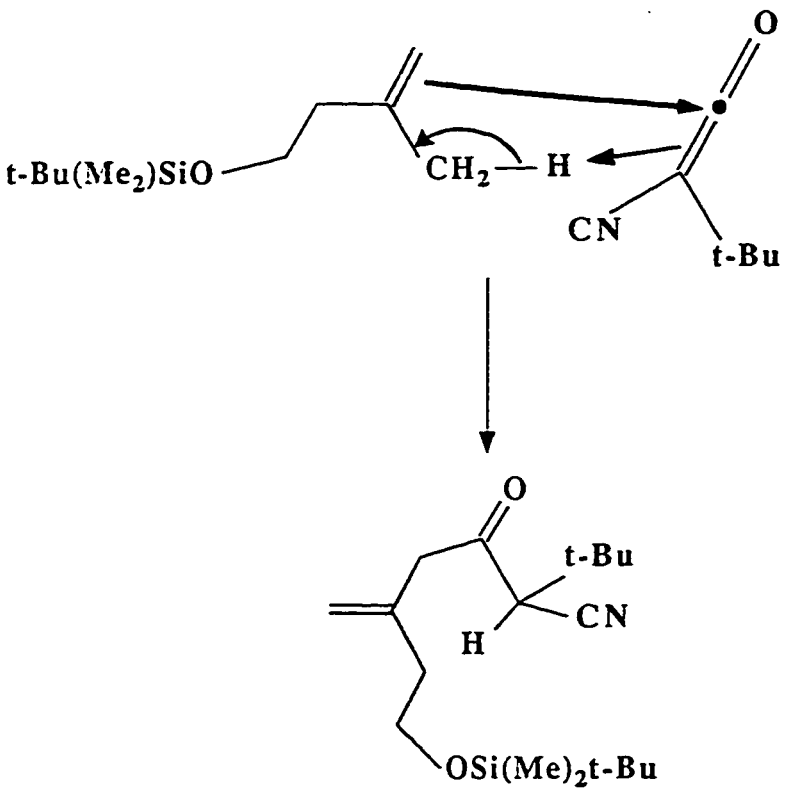
+



49

50

Scheme 23



The predominance of 49 over 50 (scheme 22) is presumably the result of steric factors in the transition state leading to 50. The assumed geometry around the double bond as shown in 50 (scheme 24) would be the outcome of the least hindered approach of TBCK towards 46.

Alkene-ketene approach as depicted in the scheme 24, would lead to the formation of 51. However, inspection of Drieding model revealed that the transition state would have severe crowding involving t-butyl of ketene and C-2 of the alkene.

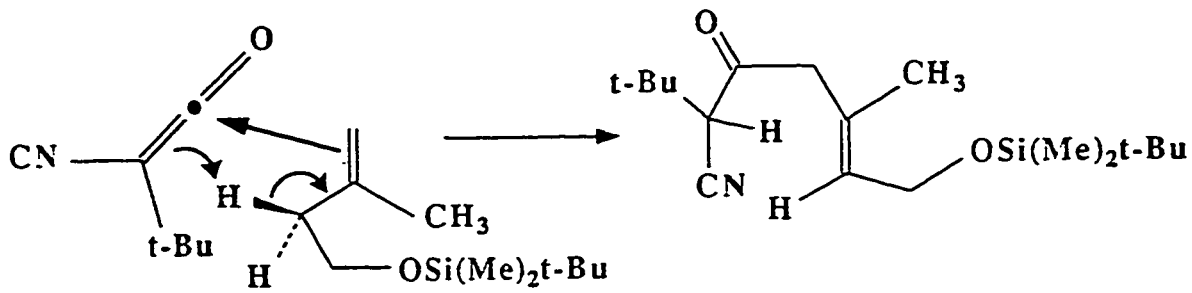
Compounds 49 and 50 are easily identifiable by their NMR spectra. The olefinic protons of 49 appeared at δ 4.92(1H, s) and 5.07(1H, bs) and the C-2 H proton appeared as a singlet at δ 3.38.

The olefinic proton of 50 appeared as a triplet (as expected) with fine allylic splitting at δ 5.44 (1H J 6.5 Hz) and the C-2 H , C-4 H_2 appeared as singlets and broad singlet, respectively, at δ 3.31 and 3.38.

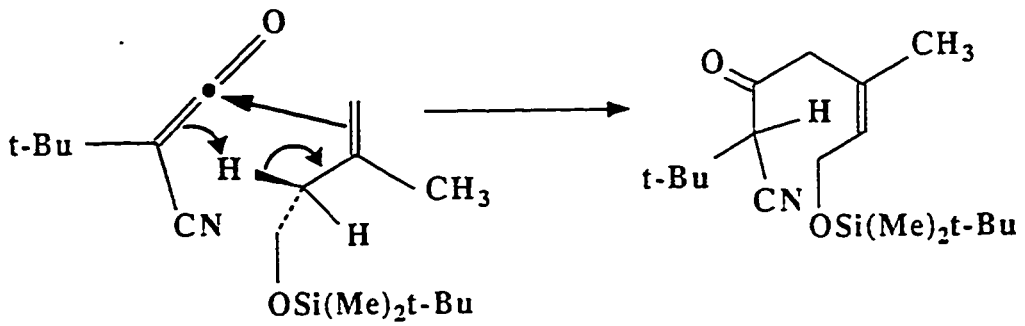
Cycloaddition of TBCK to benzyl-3-methyl-3-butenyl ether(52)

The addition of TBCK to 52 in refluxing benzene afforded 53 , 54 , and 55 in 55% yield. The isomers were separated by silica gel chromatography. The ratio of the adducts 53 , 54 , 55 was found to be 45 : 33 : 22 respectively. The reason fo assigning the stereochemistry of the major adduct as depicted in 53 is already discussed on p 38. The C-2 t-butyl of 53 is cis to the bulkier group at C-3. This would be the expected product based on the least hindered orthogonal approach of the addenda, The C-4 protons of the adduct 53

Scheme 24

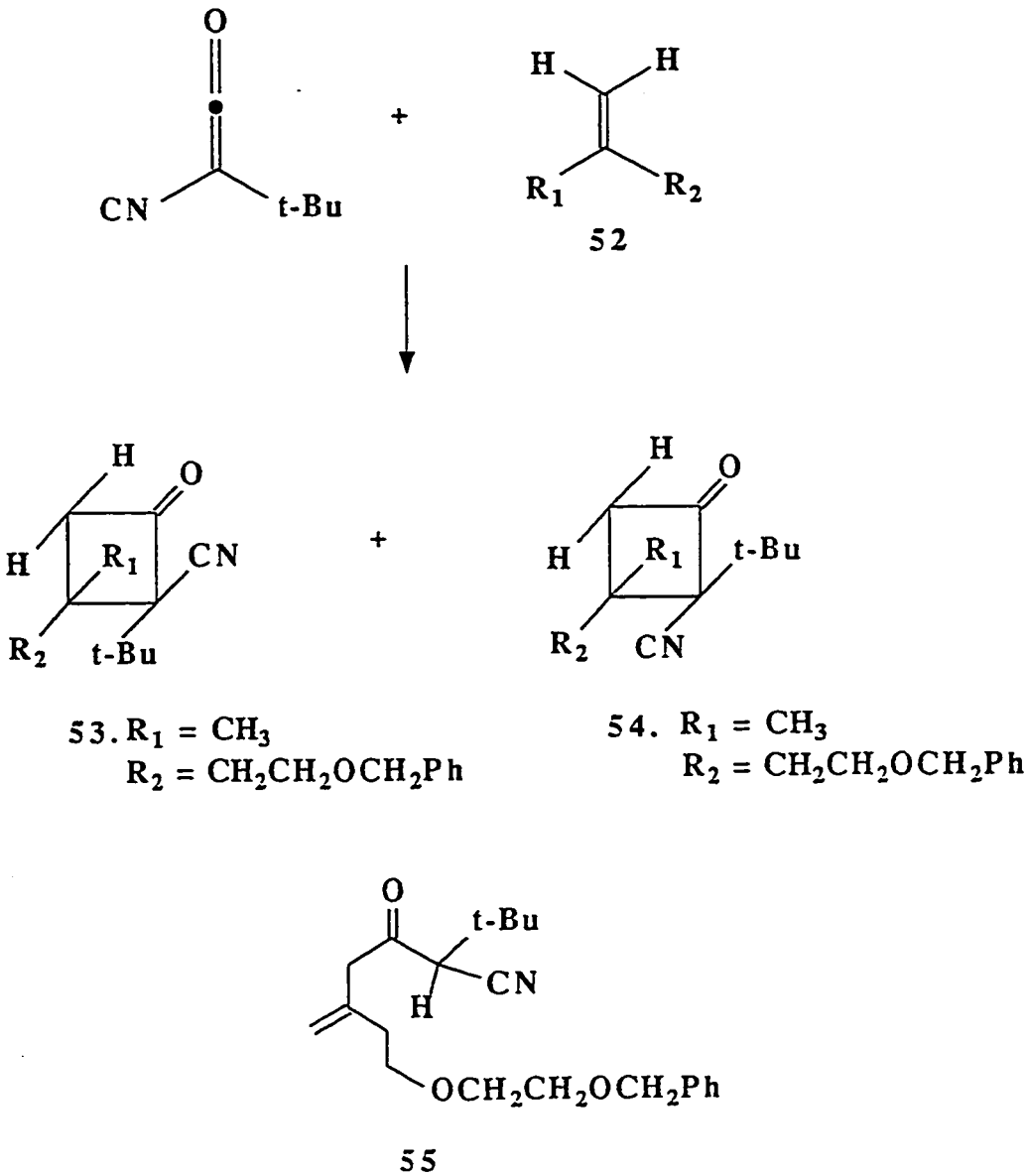


46 50



46 51

Scheme 25


O
CN
t-Bu
+
H
H
R1
R2
52
H
O
H
R1
CN
R2
t-Bu
+
H
O
H
R1
t-Bu
R2
CN
53. R1 = CH3
R2 = CH2CH2OCH2Ph
54. R1 = CH3
R2 = CH2CH2OCH2Ph
O
t-Bu
CN
H
OCH2CH2OCH2Ph
55

appeared at δ 2.78 (1H, d, A of AB type, J 17.5 Hz) and 3.30(1H, d, B of AB type, J 17.5 Hz). The corresponding protons of the other isomer 54 appeard also as doublets at δ 2.73(J 17.5) and 3.30(J 17.5).

However in addition to the cyclobutanone (53 and 54) , we also obtained compound 55.

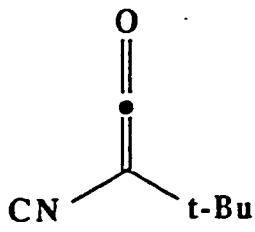
Formation of 55 is presumably a result of ene reaction as described on p 38.

Compound 55 is identified by its NMR spectrum. The olefinic protons appeared at δ 4.42(1H, bs) and 5.07(1H, bs).

Cycloaddition of TBCK to 3-methyl-3-butenyl acetate (56)

The reaction of TBCK with 56 in refluxing benzene afforded 57 , 58 , and 59 in a ratio of 42 : 35 : 23 (Scheme 27) with a total yield of 46%. We were unable to separate 57 , 58 , and 59 by silica gel column chromatography. However the structures of 57 , 58 , and 59 were deduced from the careful NMR analysis of a mixture rich in certain isomer. The stereochemistry of the compound 57 depicted is already discussed on p 38. This would be the expected product based on the least hindered orthogonal approach of the addenda. C-4 protons of the adduct 57 appeared at δ 2.80 (1H, d, A of an AB type, J 17.5 Hz) and 3.25(1H, d, A of and AB type, J 17.5 Hz). C-4 protons of the other isomer 58 also appeared as doublets (B of an AB type) at δ 2.75(J 17.5) and 3.30(J 17.5). However in addition to the cyclobutanones 57 and 58 we also obtained acyclic product 59. Formation of 59 is

Scheme 26



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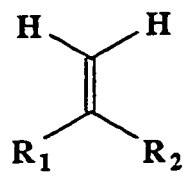
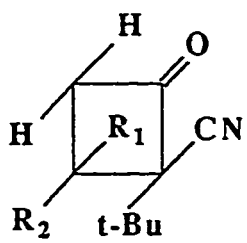


56. $R_1 = CH_3$
$R_2 = CH_2CH_2OAc$



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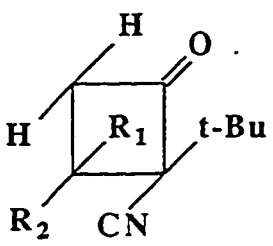
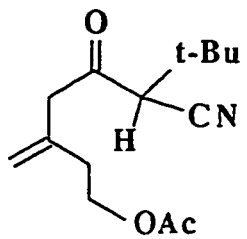


57. $R_1 = CH_3$
$R_2 = CH_2CH_2OAc$

58. $R_1 = CH_3$
$R_2 = CH_2CH_2OAc$



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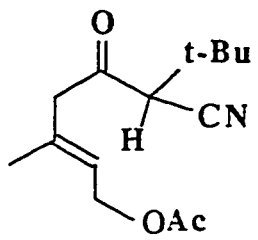


59

60

presumably a result of an ene-reaction as discussed on P 38. We could not detect the presence of an acyclic compound 60. Compound 59 is identified by its NMR spectrum in a mixture of 57 , 58 , and 59. The olefinic protons of 59 appeared at 4.98(1H, bs,) and 5.08(1H, bs).

Cycloaddition of TBCK to Benzyl-2-methyl-2-propenyl ether(61)

The reaction of TBCK with 61 in refluxing benzene afforded 62 and 63 in 42% yield. The non-separable mixture of isomers 62 and 63 were found to be in a ratio of 55:45, respectively, as determined by the integration of C-2 methyl singlets. No ene product was obtained in the reaction. The CH_2O (of C-3) of 62 and 63 appeared as AB(J 12 Hz) at δ 3.67 and 3.71 respectively. The C-3 CH_3 of 62 and 63 appeared at δ 1.53 and 1.67, respectively as singlets. The major adduct was assumed to have the stereochemistry as specified in 62 with the bulky group at C-2 and C-3 cis to each other.

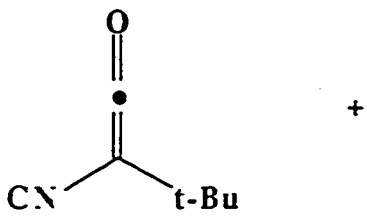
Cycloadditon of TBCK to Styrene (64)

The cycloaddition of TBCK to 64 in refluxing benzene gave 65a (scheme 28) , in 65% yield. The NMR spectra of 65a was found to be completely in agreement with the reported spectra[5-7] .

Cycloaddition of TBCK to p-Methoxy styrene(66)

To a refluxing solution of TBCK (6 mmol) was injected p-methoxy styrene 66 (6 mmol) and the reaction continued for 4 h. After the removal of the solvent the crude NMR ($CDCl_3$) spectrum of the reaction mixture

Scheme 27



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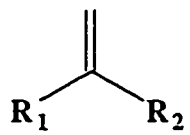
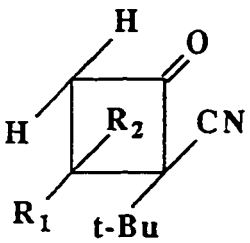


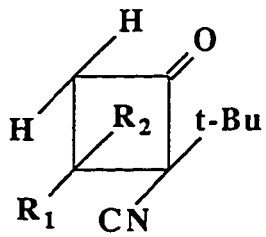
61. $R_1 = CH_3$

$R_2 = CH_2OCH_2Ph$



62. $R_1 = CH_3$

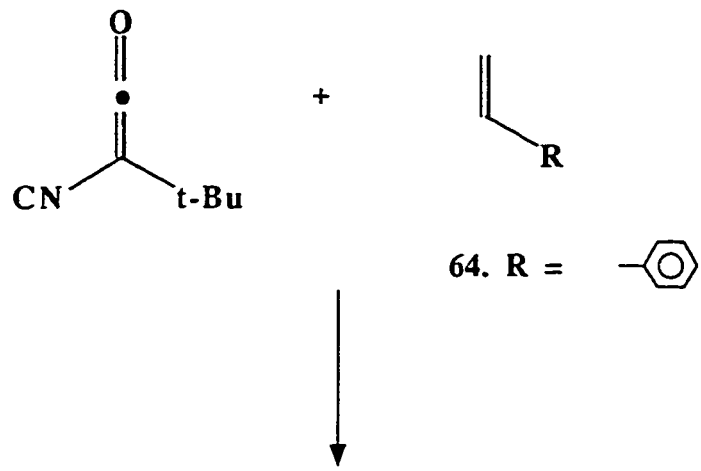
$R_2 = CH_2OCH_2Ph$



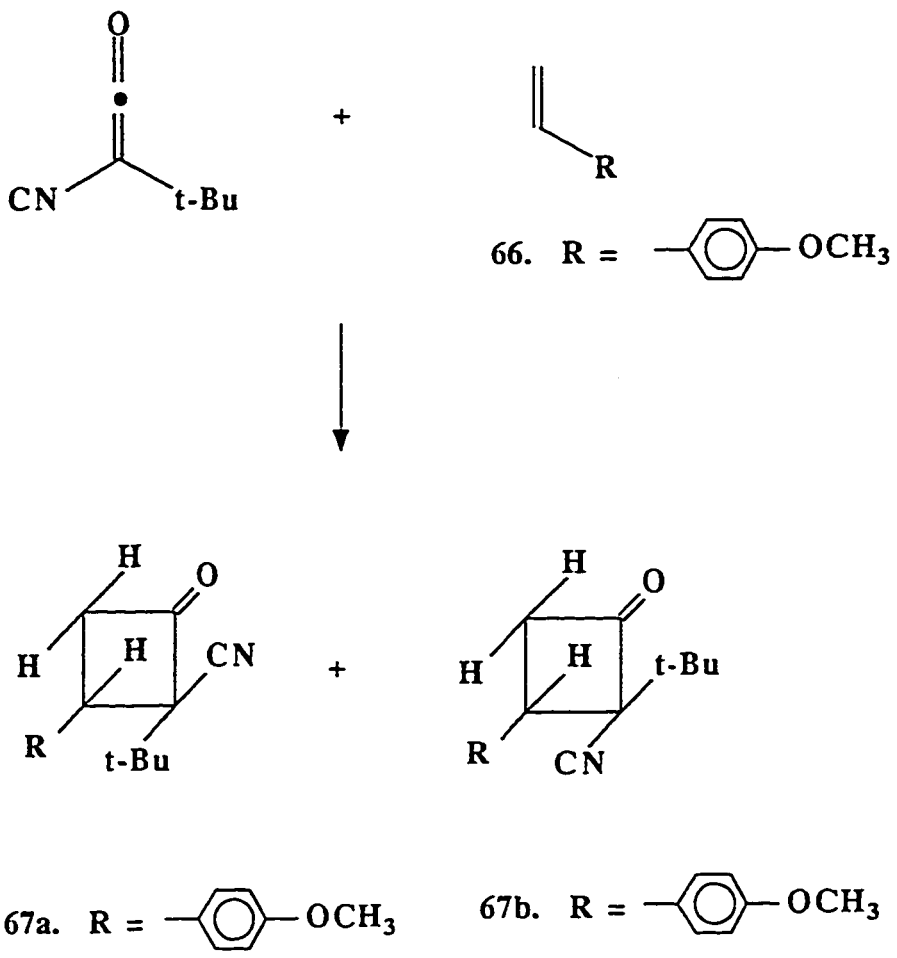
63. $R_1 = CH_3$

$R_2 = CH_2OCH_2Ph$

Scheme 28



Scheme 29


O
CN
t-Bu
+
R
66. R =
OCH3
H
O
H
H
CN
R
t-Bu
+
H
O
H
H
t-Bu
R
CN
67a. R =
OCH3
67b. R =
OCH3

revealed the presence of two isomers 67a and 67b in a ratio of 40 : 60 as determined by the integration of t-Butyl protons at δ 0.90 and 1.20 respectively. The C-3 H of 67a appeared downfield, as expected, at δ 4.38 (t, J 10.5). The silica gel chromatography using hexane/ether (10 : 1) as eluent gave a pure sample of 67b followed by a mixture of 67a and 67b as colourless liquid.

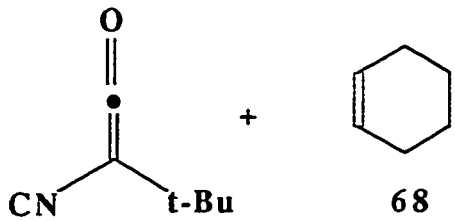
Cycloaddition of TBCK to cyclohexene (68)

Reaction of TBCK with 68 (scheme 30) in refluxing toluene resulted in 69 as reported by Moore.[17] However the pure 69 was obtained by column chromatography using 10 : 1 (hexane/ether) as eluent. The NMR data of 69 is in complete agreement with the reported data by Moore[17]

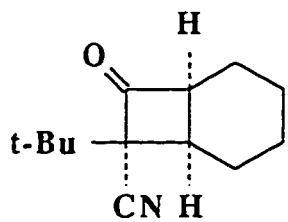
Cycloaddition of TBCK to variety of alkynes(70a-70f)

The cycloaddition of TBCK and 70a (scheme 31) in refluxing benzene afforded 71a in good yield. The olefinic proton of 71a appeared at δ 6.15. However the addition reaction of TBCK and 70b in benzene at various temperature and several trials afforded 71b in minor quantities. The olefinic proton of 71b appeared at δ 6.15(J 1.8) as a triplet. The corresponding reaction of TBCK with 70c at 20°C , 50° C , and 80°C in benzene again gave only minute quantities of 71c . Repeated trails failed to yield appreciable quantities of the cycloadduct. The NMR spectrum of the crude reaction mixture displayed a 1H, triplet at δ 6.17(J 1.8 Hz). Similar reaction with 70d , 70e and 68f at 20° C, 50° C, and 80° C, and even in refluxing benzene for

Scheme 30

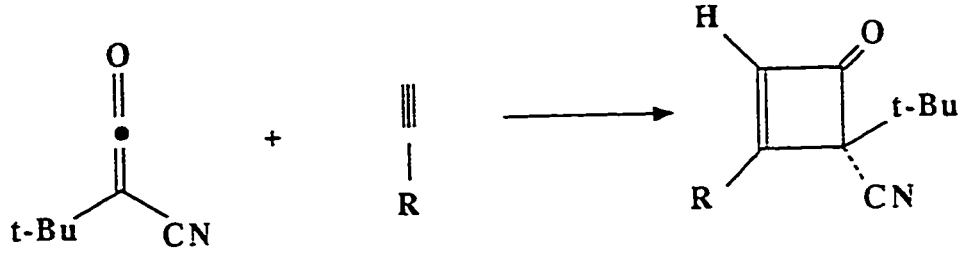


68



69

Scheme 31



70 71

a. R = —Ph

b. " —$(CH_2)_3CH_3$

c. " —$(CH_2)_5CH_3$

d. " —$CH_2OSi(Me)_2t\text{-}Bu$

e. " —$C(Me)_2OSi(Me)_2t\text{-}Bu$

f. " —$CH_2O\,CH_2Ph$

shorter or longer duration failed to give any identifiable cycloadduct.

Most probably the addition reactions with terminal aliphatic alkynes are either very slow at low temperatures or the highly strained adducts 71 formed at higher temperature may not survive the relatively harsh reaction conditions.

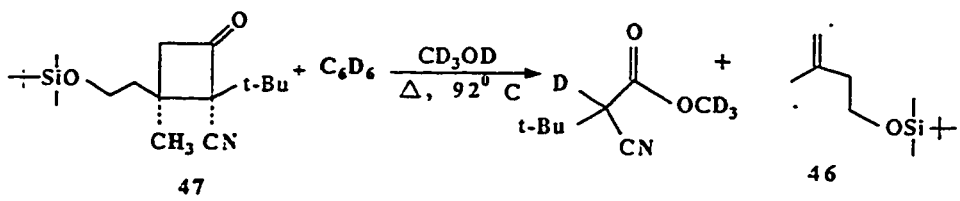
3.2 Thermal Study of Various Cyclobutanones

Thermal Study of Cycloadduct (47)

Cycloreversion of the adduct 47 was followed by proton NMR technique, which offers a convenient method for following their reaction. In the NMR tube a C_6D_6 solution of the adduct 47 was taken along with the trapping agent CD_3OD which captures the ketene (TBCK) immediately upon its formation. Using the integration of protons of 46 and the C-2 t-Bu and C-3 methyl of 47 , the concentration of adduct 47 was determined from time to time (Table 1) and the first order rate constant was determined by linear regression analysis (Fig. 1). The rate constant (k) for the cycloreversion of 47 in C_6D_6 was found to be $9.2 \times 10^{-5}\ s^{-1}$ (Fig. 1). The corresponding rate constants, k, in solvent CD_3OD and DMSO-d_6, were determined to be 22×10^{-5} (Fig. 3, Table 11) and $1.7 \times 10^{-4}\ s^{-1}$ (Fig. 2, Table 11)respectively. The rate constants, k, in C_6D_6 , DMSO-d_6 , and CD_3OD were, thus, found to be in a ratio of 1.0 : 1.8 : 2.4, respectively. Such a small solvent certifies the molecular nature of the cycloreversion process. For the cycloaddition or cycloreversion process to be a stepwise reaction involving a zwitterion

Table 1 : Cycloreversion of 47 in C_6D_6 at 92°C in the Presence of CD_3OD

S. No.	Time (Minutes)	[47]	ln [47]	[46]	% 47 Decomposed
1	0	0.181	-1.709	0	0
2	60	0.141	-1.959	0.040	22
3	120	0.117	-2.145	0.633	35
4	180	0.087	-2.443	0.094	52
5	240	0.076	-2.577	0.105	58
6	300	0.040	-3.220	0.141	78
7	360	0.027	-3.830	0.159	88



47 46

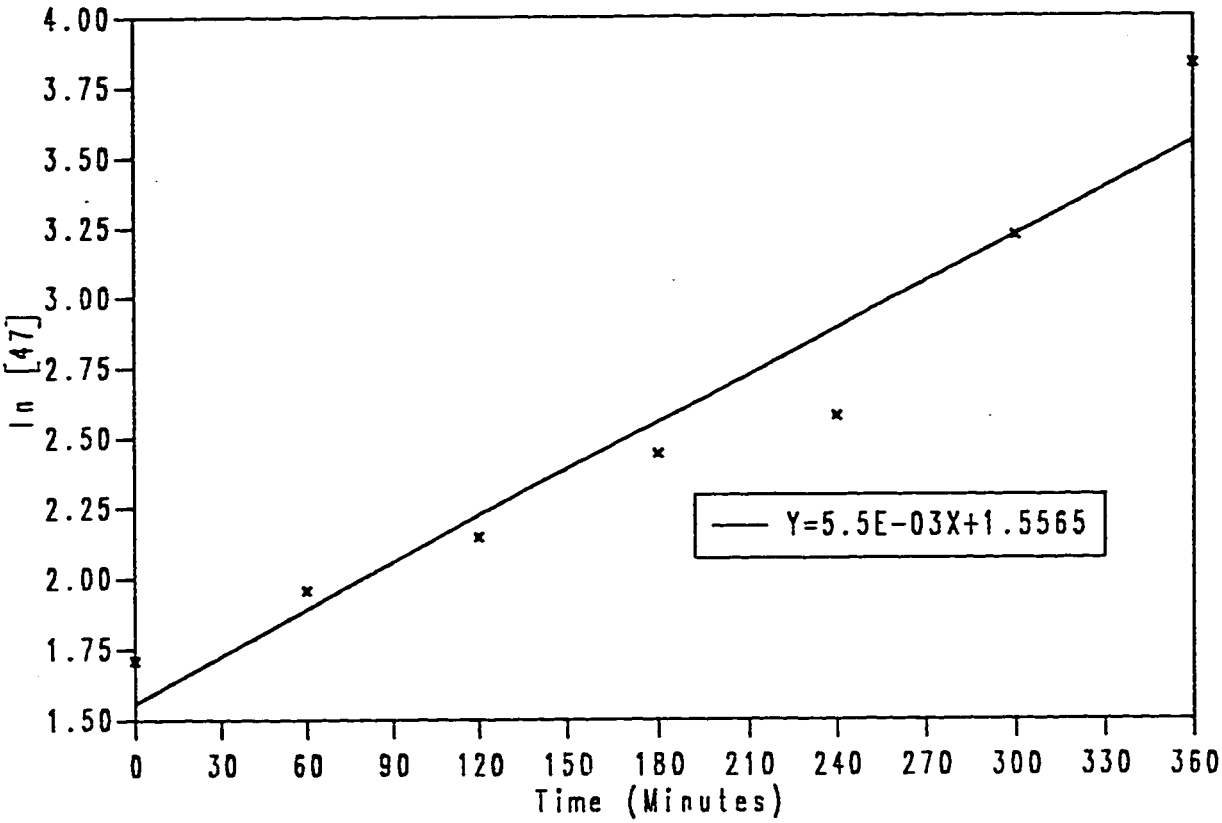
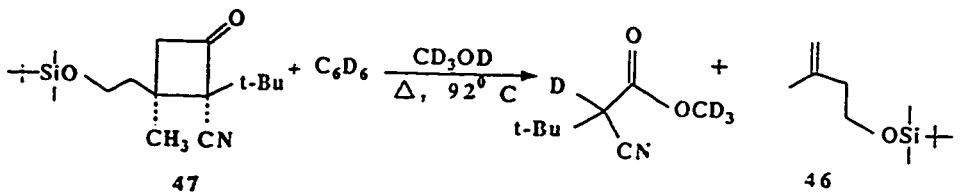


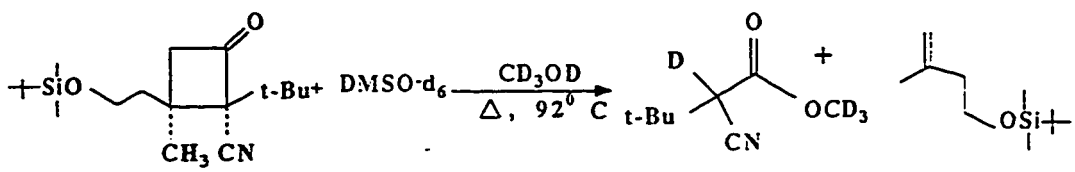
Fig. 1 : Method of Integration; Analysis of Results for First-Order Reaction. Plot of ln [47] Against Time.



47 46

Table 2 : Cycloreversion of 47 in DMSO-d_6 at 92°C in the Presence of CD_3OD

S. No.	Time (Minutes)	[47]	ln [47]	[46]	% 47 Decomposed
1	0	0.1810	-1.71	0	0
2	30	0.1470	-1.92	0.034	18.5
3	60	0.1220	-2.10	0.059	32.5
4	90	0.0778	-2.55	0.110	57.0
5	120	0.0600	-2.81	0.121	66.6
6	150	0.0415	-3.18	0.139	77.0



47 46

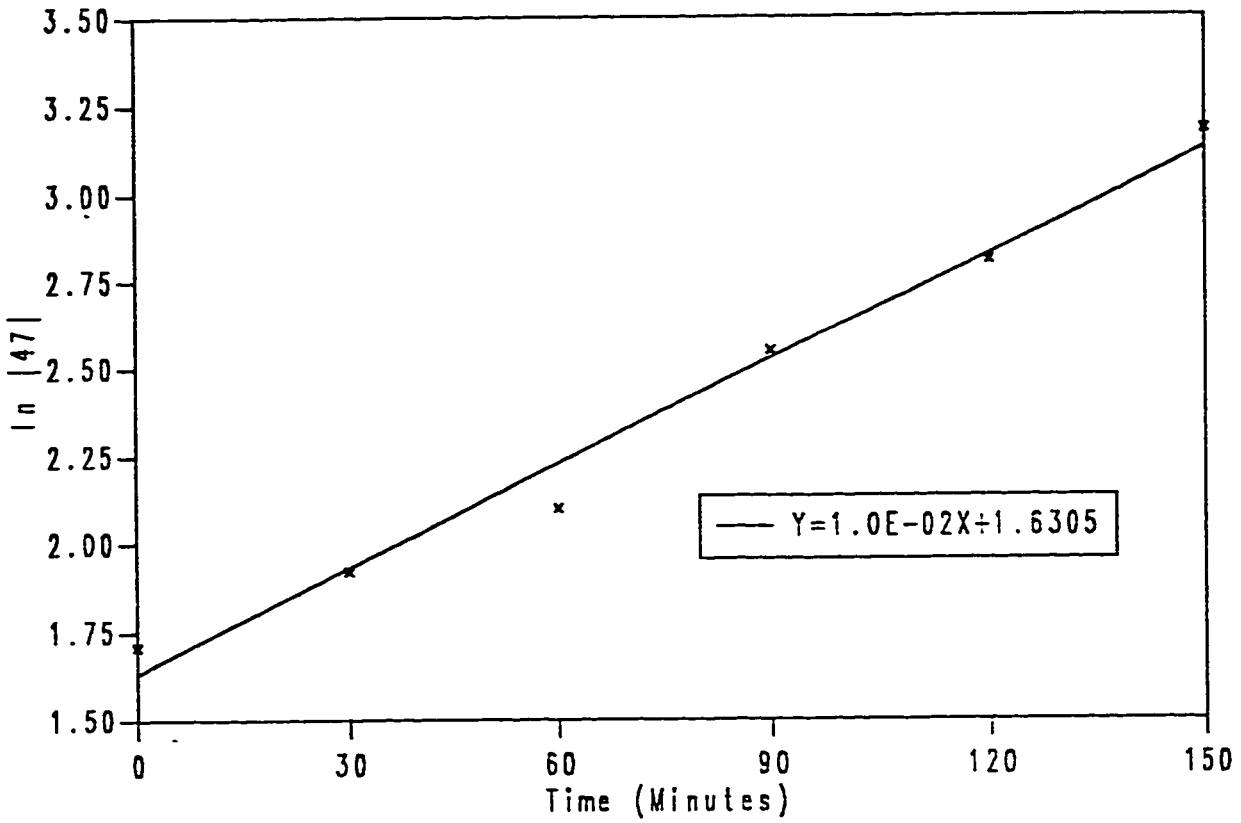


Fig. 2 : Method of Integration; Analysis of Results for First-Order Reaction. Plot of ln [47] Against Time.

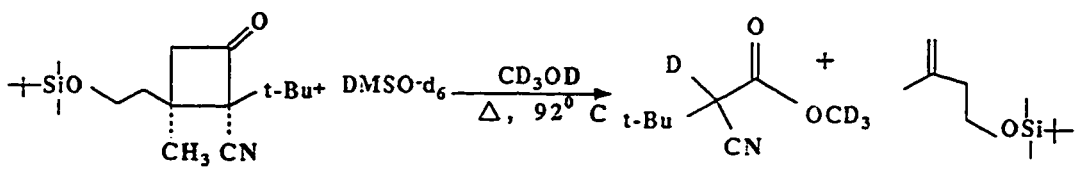
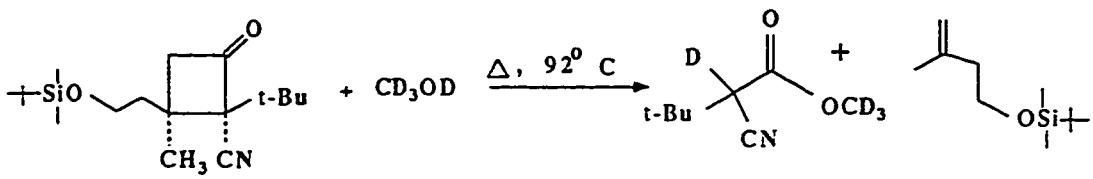


Table 3 : Cycloreversion of 47 in CD_3OD at 92°C

S. No.	Time (Minutes)	[47]	ln [47]	[46]	% 47 Decomposed
1	0	0.1810	-1.71	0	0
2	30	0.1290	-2.05	0.052	29
3	50	0.0878	-2.43	0.092	51
4	110	0.0514	-3.00	0.130	72
5	170	0.0181	-4.01	0.163	90



47 46

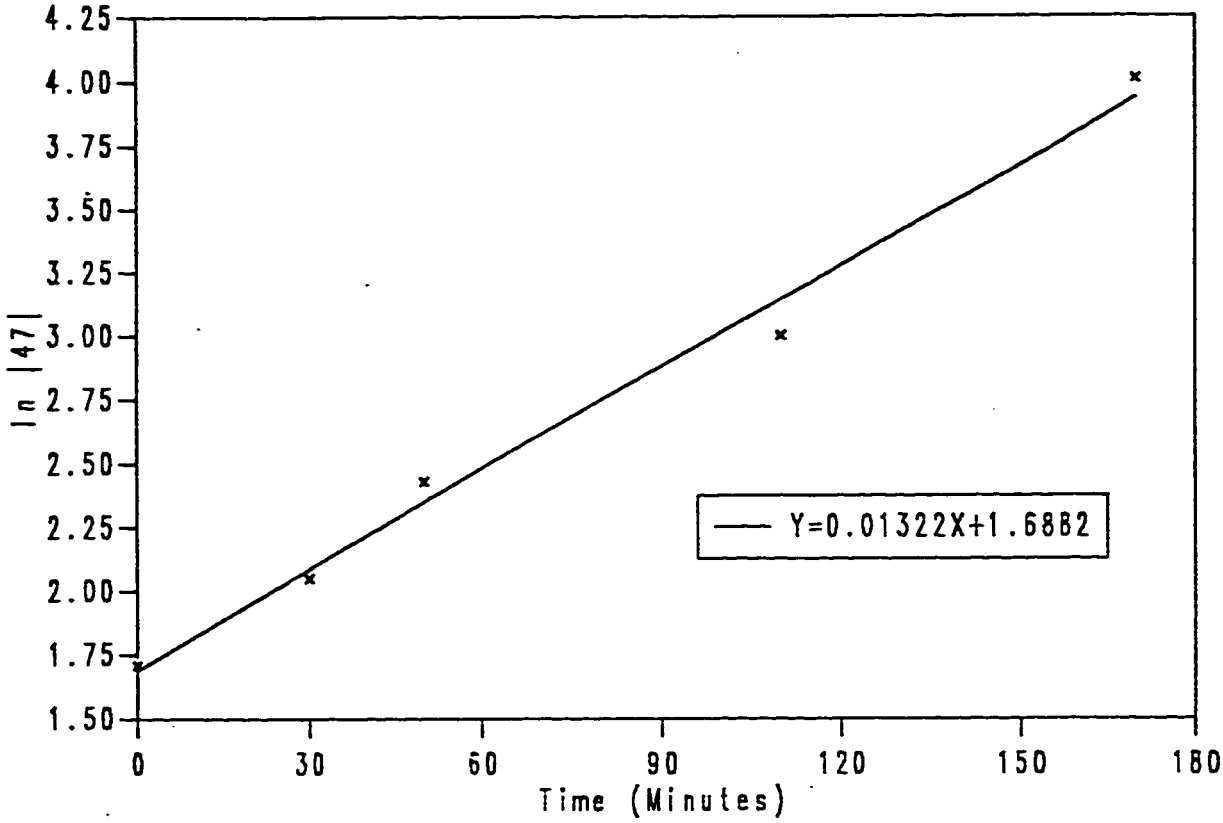
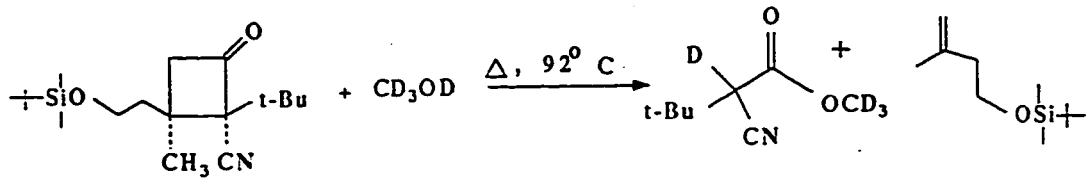


Fig. 3 : Method of Integration; Analysis of Results for First-Order Reaction. Plot of ln [47] Against Time.



47 46

intermediate, one would expect a much larger solvent effect.

Thermal Study of (45)

The cycloreversion of cycloadduct 45 was followed as described earlier by NMR technique. The results of the reaction are tabulated (Table 4). The cycloreversion did not happen at 92° C. Even at higher temperatures it was indeed a slow process. The rate constant, k, at 120° C in C_6D_6 was found to be $6.8 \times 10^{-6}\ s^{-1}$ (Fug. 4, Table 11).

Thermal study of (65a)

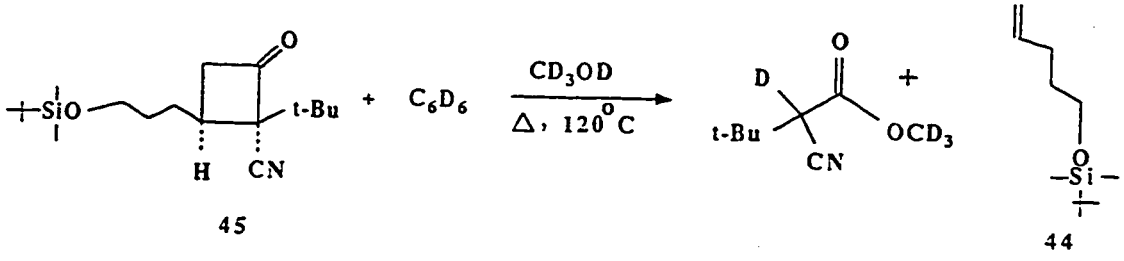
Cycloreversion of 65a was followed by NMR technique as described before. The integration of C-3 H of the adduct 65a and the olefinic protons of 64 was used to determine the concentration of 65a at different intervals of time. The results are tabulated (Table 5). The rate constants, k, at 92°C in C_6D_6 and CD_3OD were found to be 3.3×10^{-4} (Fig. 5, Table 11) and $2.6 \times 10^{-4}\ s^{-1}$, (Fig. 6, Table 11) respectively. The independency of the cycloreversion on solvents with a wide difference in dielectric constants, thus confirms the concerted nature of the mechanism.

Thermal study of (65b)

The cycloreversion of styrene cycloadduct 65b was found to be much slower compare to the corresponding cycloadduct 65a. The rate constant k of 65b in C_6D_6 at 120° C was found to be $3.3 \times 10^{-6}\ s^{-1}$ (Fig. 7, Table 11).

Table 4 : Cycloreversion of 45 in C_6D_6 at 120° in the Presence of CD_3OD

S. No.	Time (Hours)	[45]	ln [45]	[44]	% 45 Decomposed
1	0.0	0.310	-1.171	0	0
2	2.0	0.291	-1.234	0.019	6
3	4.5	0.279	-1.277	0.031	10
4	9.0	0.242	-1.419	0.068	22
5	13.5	0.223	-1.501	0.087	28
6	18.5	0.202	-1.600	0.108	35
7	23.0	0.177	-1.732	0.133	43
8	27.5	0.155	-1.864	0.155	50



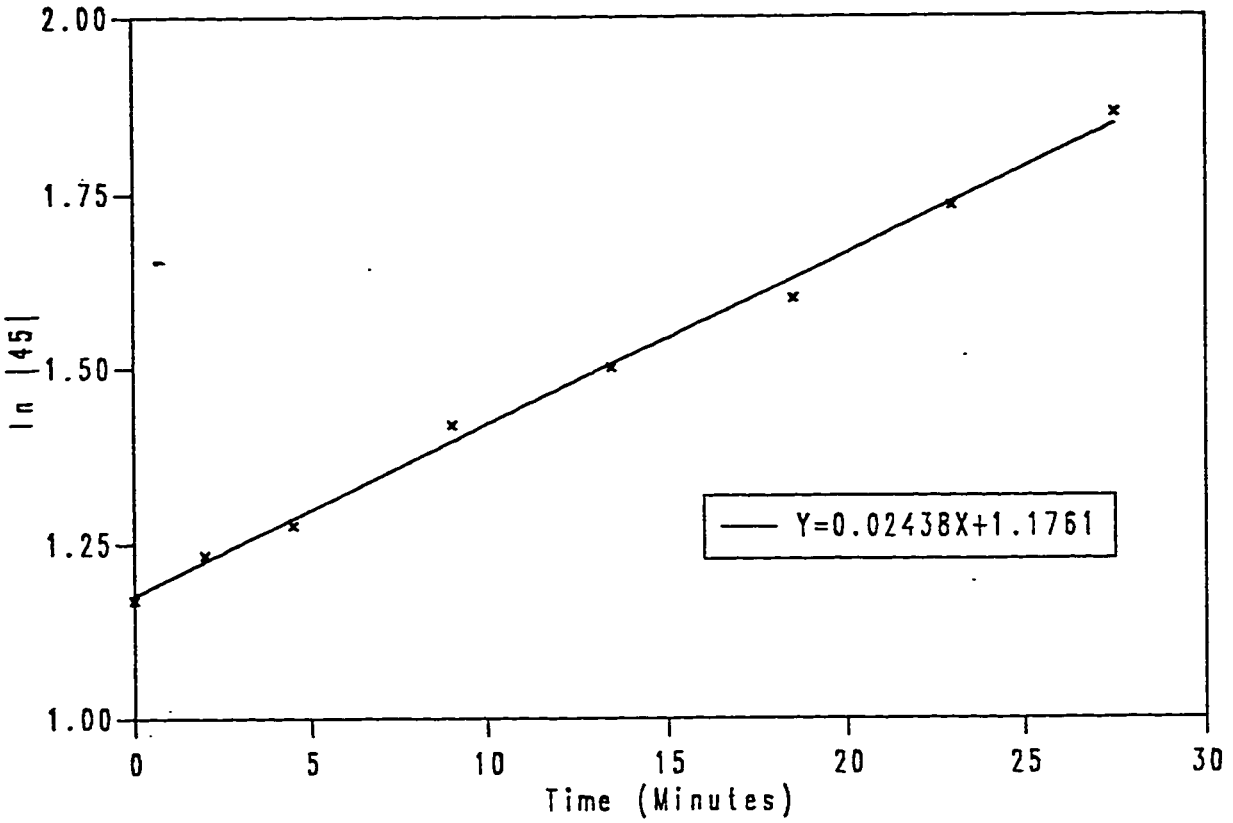
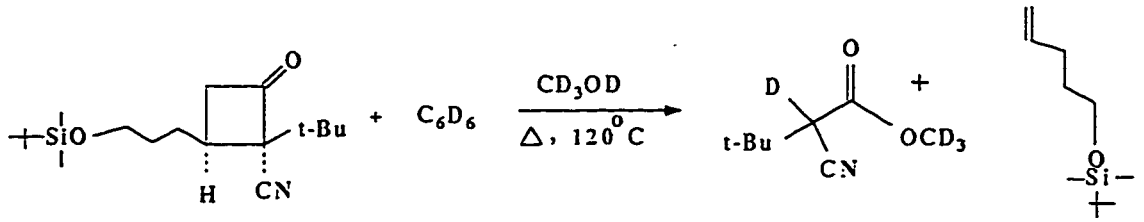


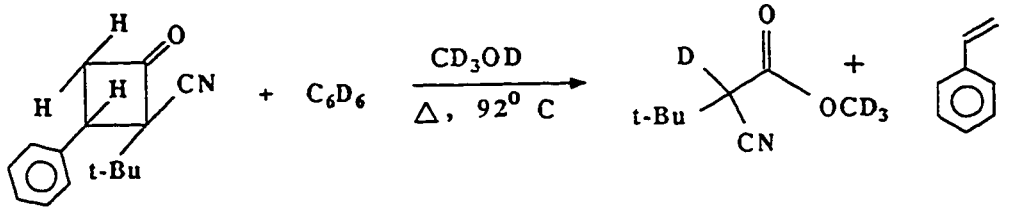
Fig. 4 : Method of Integration; Analysis of Results for First-Order Reaction. Plot of ln [45] Against Time.



45 44

Table 5 : Cycloreversion of 65a at 92°C in C_6D_6 in the Presence of CD_3OD

S. No.	Time (Minutes)	[65a]	ln [65a]	[64]	% 65a Decomposed
1	0	0.264	-1.33	0	0
2	15	0.203	-1.59	0.061	23
3	30	0.148	-1.91	0.116	44
4	45	0.124	-2.09	0.132	53
5	66	0.066	-2.72	0.198	75



65a 64

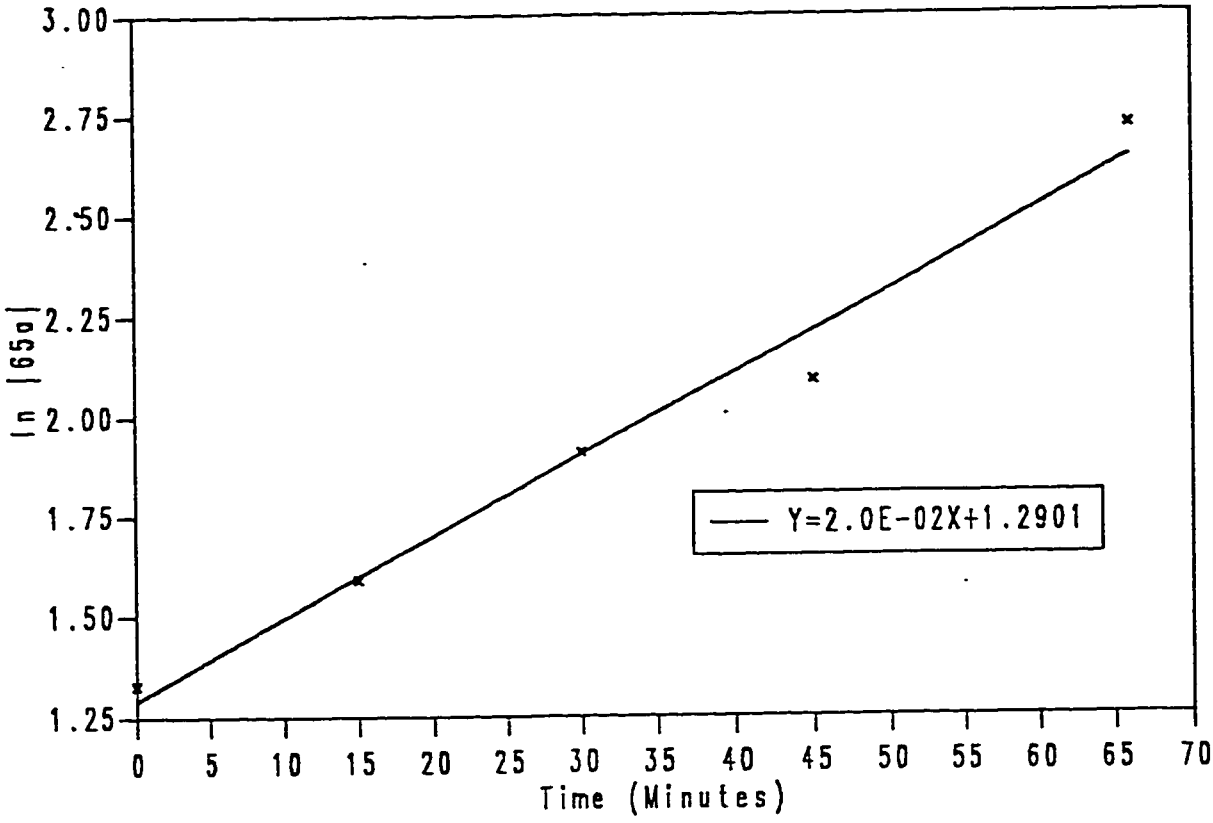
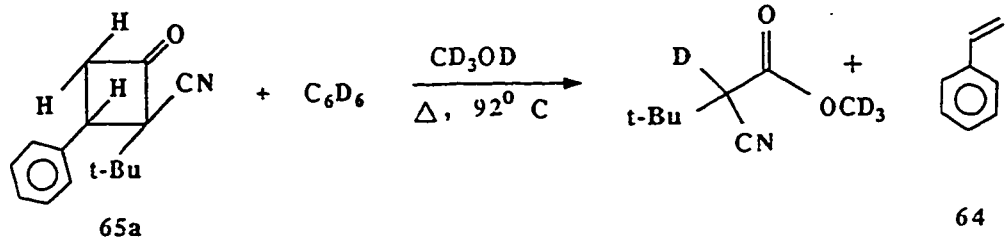


Fig. 5 : Method of Integration; Analysis of Results for First-Order Reaction. Plot of ln [65a] Against Time.

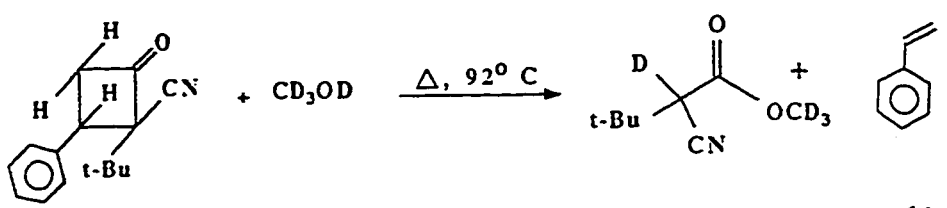


65a

64

Table 6 : Cycloreversion of 65a in CD_3OD at 92°C

S. No.	Time (Minutes)	[65a]	ln [65a]	[64]	% 65a Decomposed
1	0	0.264	-1.33	0	0
2	15	0.211	-1.56	0.053	20
3	30	0.158	-1.84	0.106	40
4	45	0.129	-2.05	0.135	51
5	60	0.103	-2.27	0.161	61



65a 64

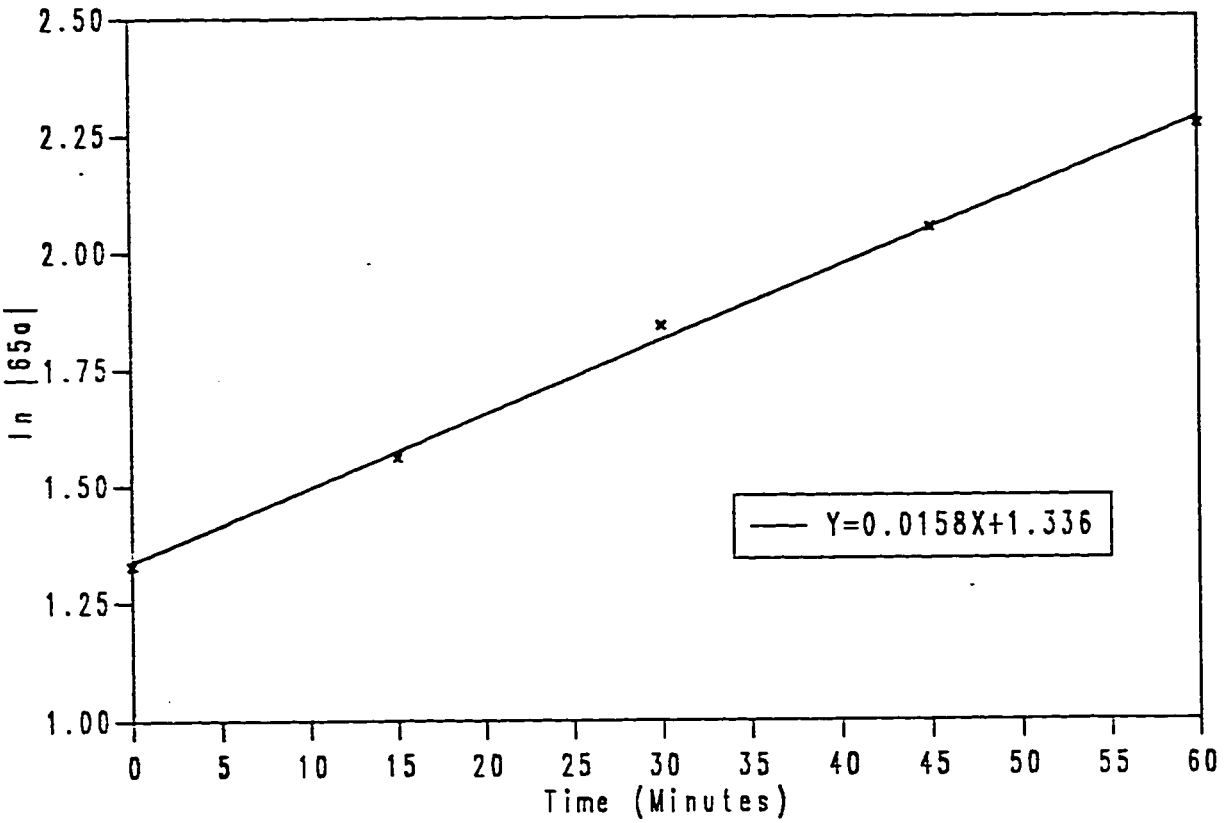
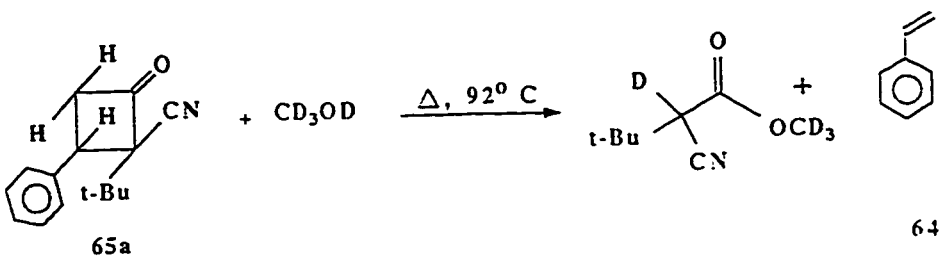


Fig. 6 : Method of Integration; Analysis of Results for First-Order Reaction. Plot of ln [65a] Against Time.

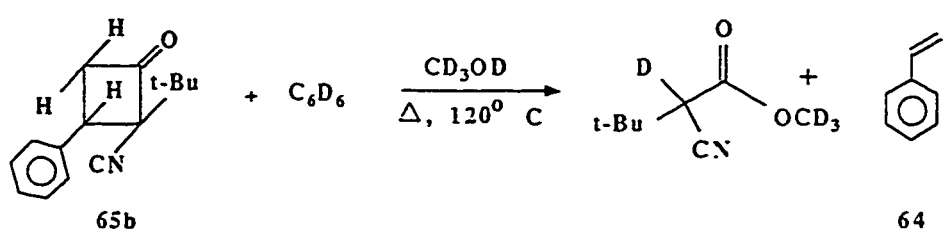


65a

64

Table 7 : Cycloreversion of 65b in C_6D_6 at 120°C in the Presence of CD_3OD

S. No.	Time (Hours)	[65b]	ln [65b]	[64]	% 65b Decomposed
1	0	0.264	-1.33	0	0
2	3.5	0.254	-1.37	0.010	3.9
3	5.5	0.247	-1.40	0.017	6.4
4	7.5	0.242	-1.42	0.022	8.4
5	9.5	0.238	-1.44	0.026	10.0



65b 64

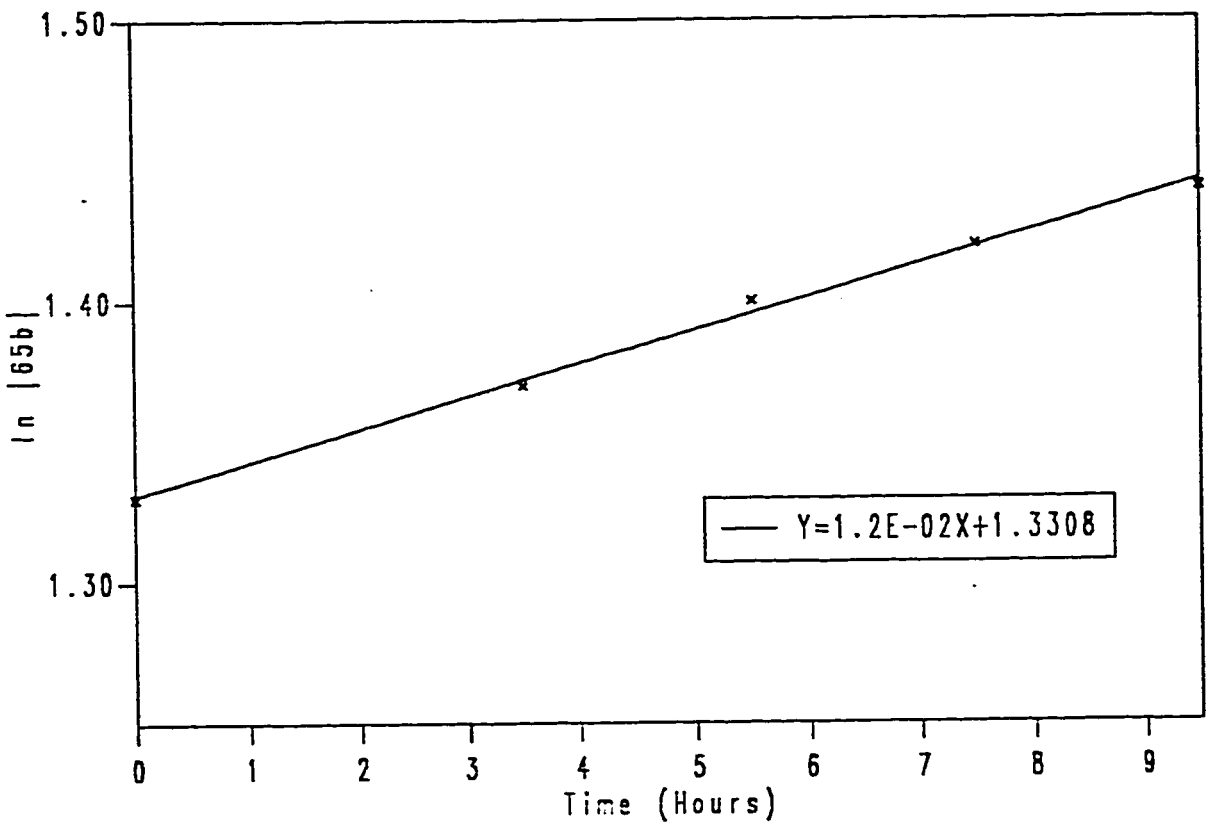
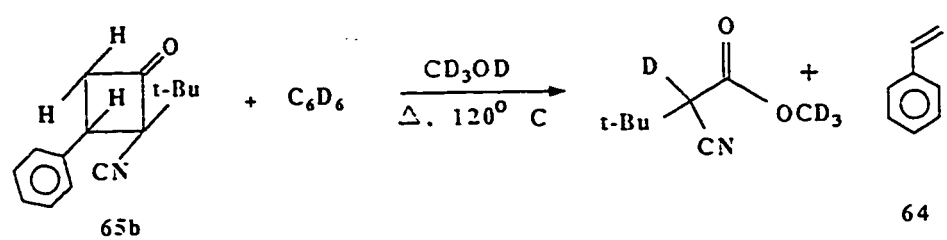


Fig. 7 : Method of Integration; Analysis of Results for First-Order Reaction. Plot of ln [65b] Against Time.



65b

64

Thermal Study of (67b)

While the styrene adduct 65b underwent cycoreversion cleanly at 120° C, the corresponding process for the compound 67b was too slow to measure at 92° C. The cyclreversion did not happen at this temperature. However the rate constant, k, at 120° C in C_6D_6 was found to be $9.7 \times 10^{-5} s^{-1}$ (Fig. 8, Table 11).

Thermal Study of (69)

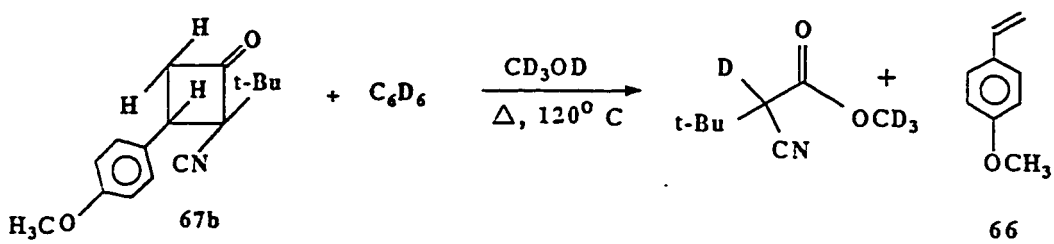
The cycloreversion of 69 was studied in C_6D_6 at 92° C and was found to be very slow to measure. However, the process happened at higher temperature. Using integration of C-2 t-Bu of and 69 , t-buyl of trapped ketene, TBCK, and olefinic protons of cyclohexene, the concentration of 69 at different times are determined. The results are tabulated in Table 11. The rate constant, k, at 103° C and 120° C were found to be 1.1×10^{-5} (Fig. 9, Table 11) and 5.8×10^{-5} (Fig. 10, Table 11) respectively.

Cycloaddition of TBCK with trans,trans 2,4-hexadiene is reported to give 73 instead of 74 which would have been the result of a concerted process (scheme 32). Thus a stepwise mechanism involving a zwitterionic intermediate 72 may be involved. The addition of TBCK to cyclohexadiene 75 (Scheme 33) resulted in the formation of the cyclbutanone 76 (71%) and the bicyclic enol ether 77 (29%).

Furthermore it was observed that 76 could be converted into 77 upon thermolysis. However it has not been determined if this transformation is a

Table 8 : Cycloreversion of 67b in C_6D_6 at 120°C

S. No.	Time (Hours)	[67b]	ln [67b]	[66]	% 67b Decomposed
1	0	0.321	-1.14	0	0
2	1	0.225	-1.49	0.096	30
3	2	0.165	-1.80	0.157	49
4	3	0.120	-2.12	1.990	62
5	4	0.076	-2.58	0.244	76



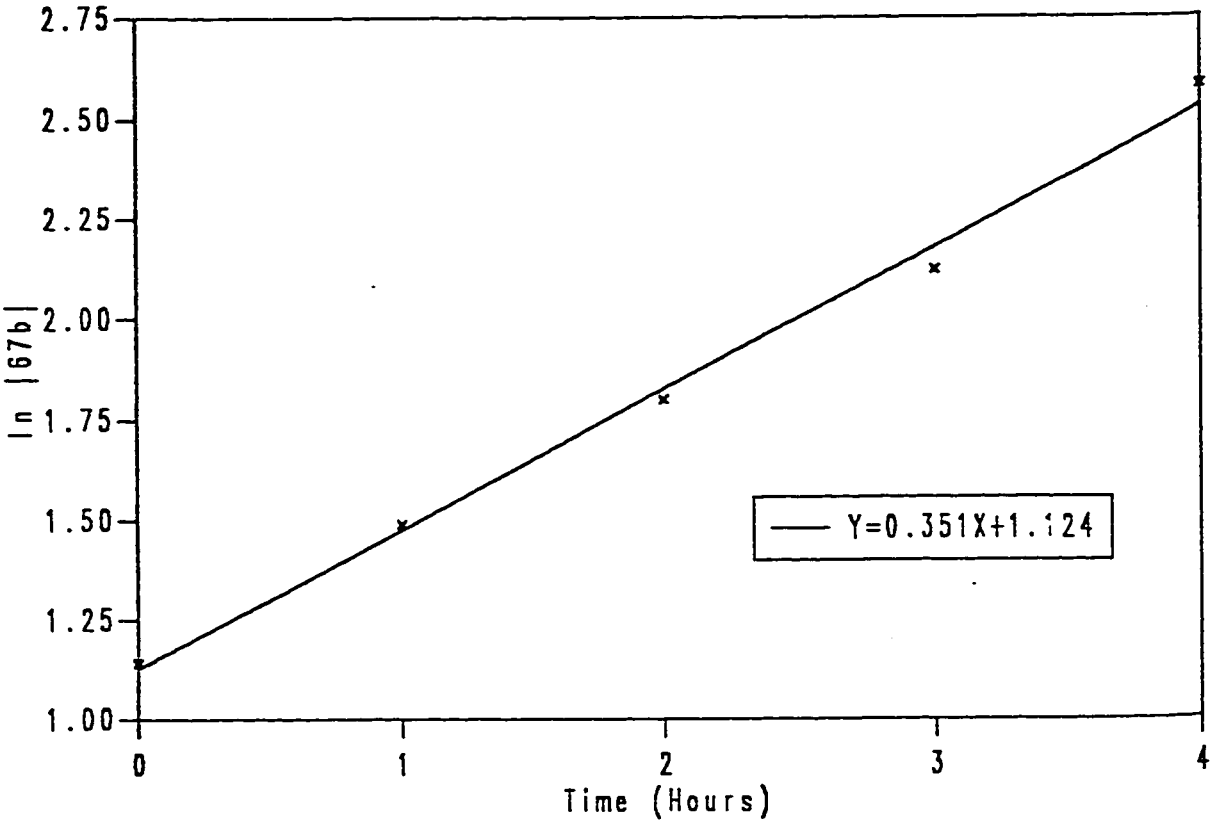


Fig. 8 : Method of Integration; Analysis of Results for First-Order Reaction. Plot of ln [67b] Against Time.

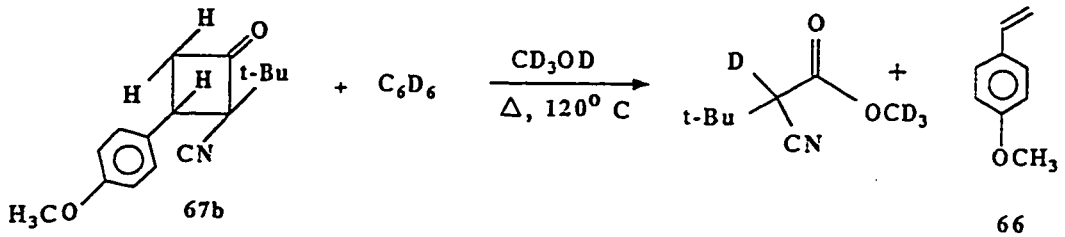
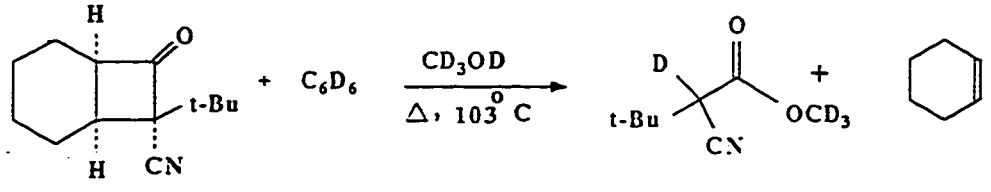


Table 9 : Cycloreversion of 69 in C_6D_6 at 103° in the Presence of CD_3OD

S. No.	Time (Hours)	[69]	ln [69]	[68]	% 69 Decomposed
1	0	0.146	-1.92	0	0
2	1	0.138	-1.98	0.0073	5
3	2	0.135	-2.00	0.0102	7
4	2.5	0.132	-2.03	0.0146	10
5	4	0.126	-2.07	0.0204	14



69 68

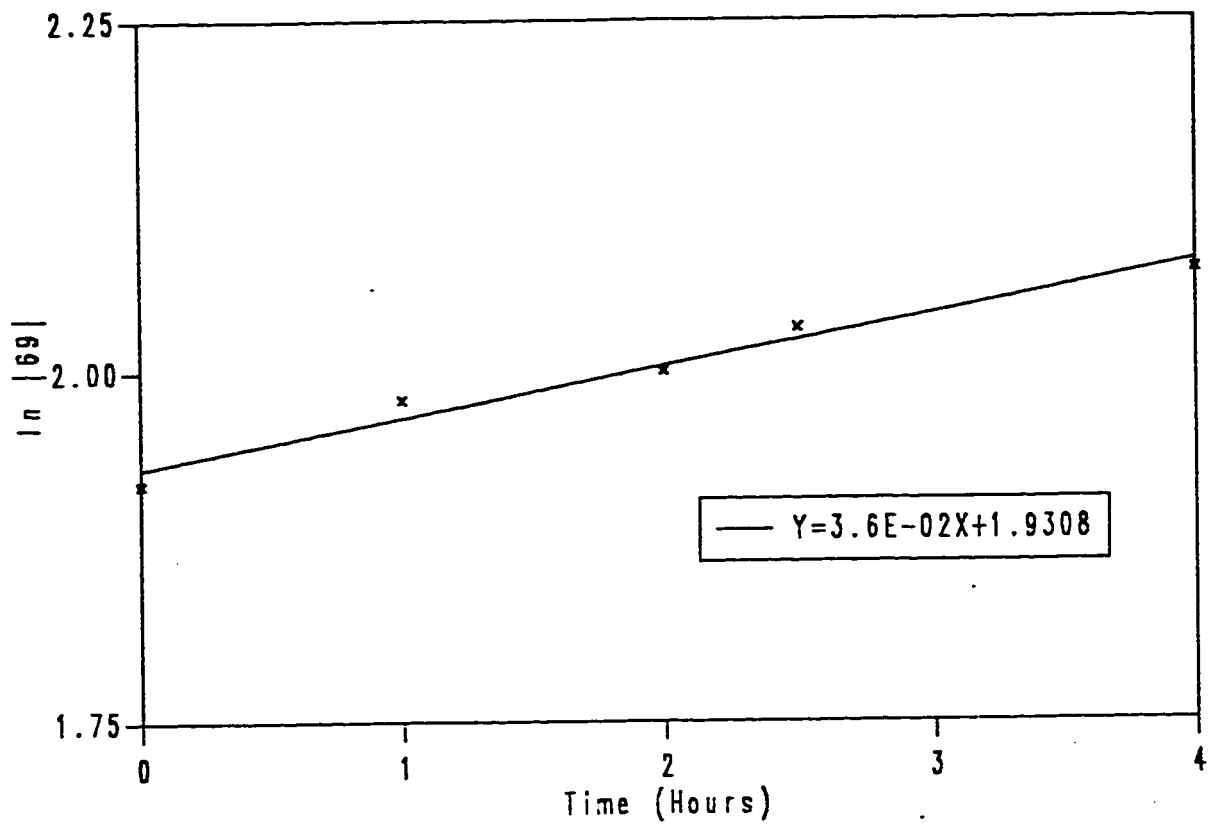
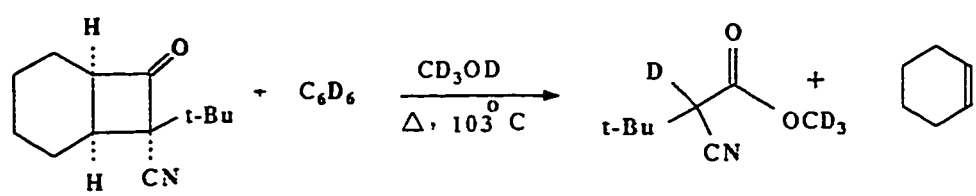


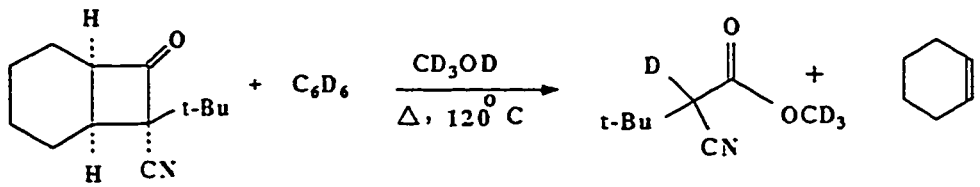
Fig. 9 : Method of Integration; Analysis of Results for First-Order Reaction. Plot of ln [69] Against Time.



69 68

Table 10 : Cycloreversion of 69 in C_6D_6 at 120°C in the Presence of CD_3OD

S. No.	Time (Hours)	[69]	ln [69]	[68]	% 69 Decomposed
1	0	0.1260	-2.07	0	0
2	1	0.1010	-2.29	0.0240	20
3	2	0.0806	-2.52	0.0450	36
4	3	0.0689	-2.68	0.0567	45
5	4	0.0523	-2.95	0.4800	48



69 68

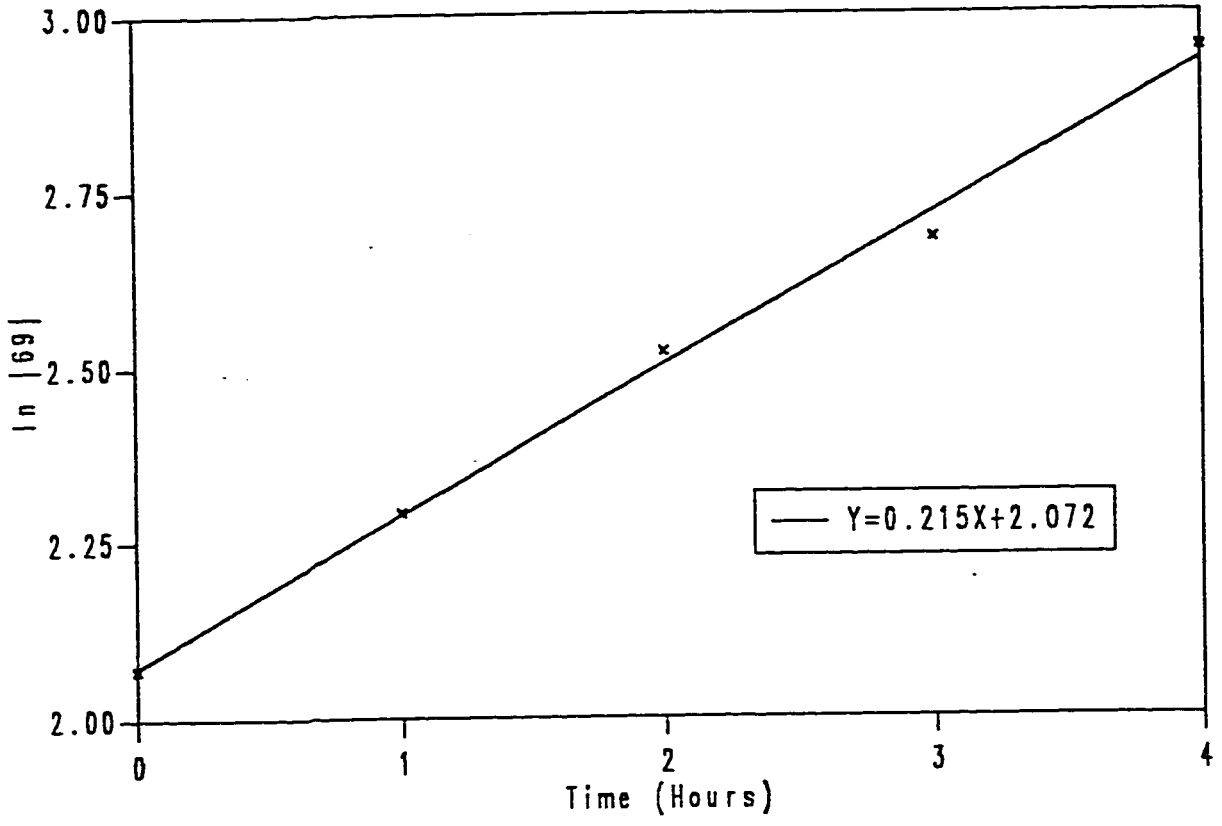
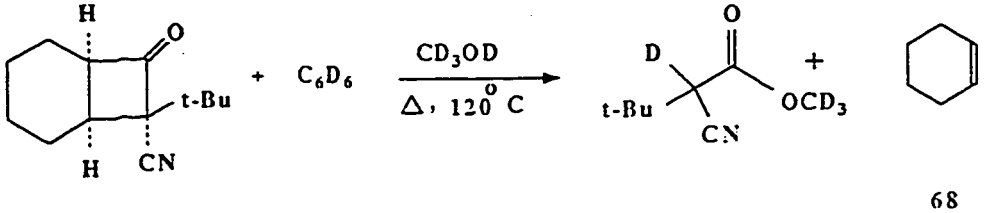


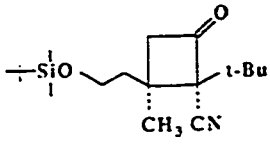
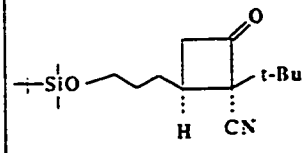
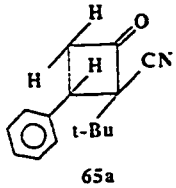
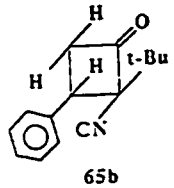
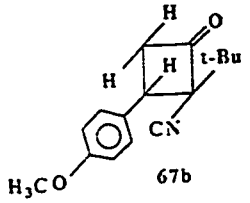
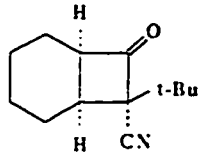
Fig. 10 : Method of Integration; Analysis of Results for First-Order Reaction. Plot of ln [69] Against Time.



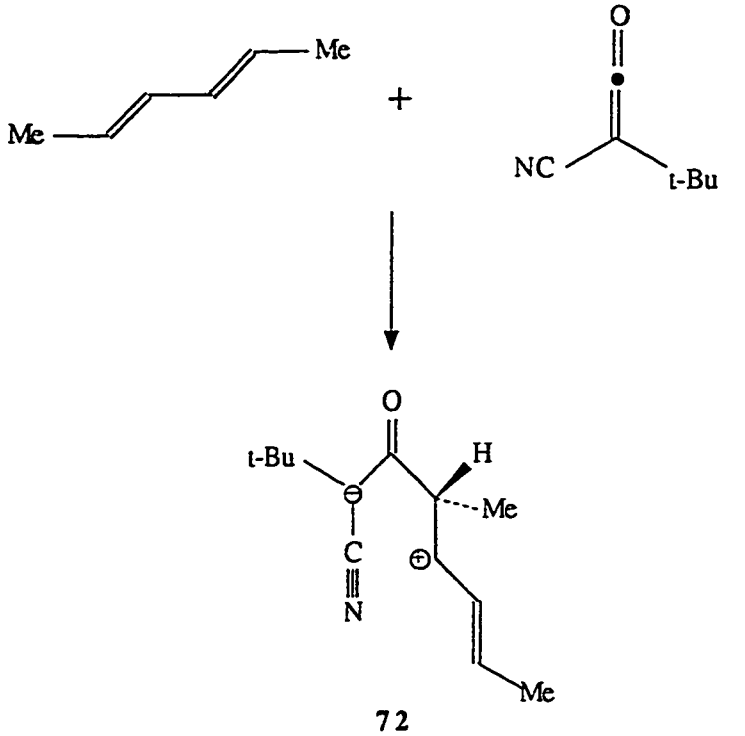
69

68

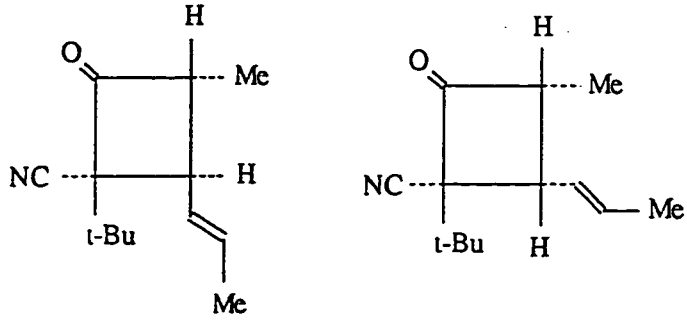
Table 11 : First Order Rate Constants of Various Cyclobutanones.

Adduct	Temp °C	Solvent	k (10^{-5} s^{-1})
 47	92 92 92	C_6D_6 DMSO-d_6 CD_3OD	9.2 17 22
 45	120	C_6D_6	0.68
 65a	92 92	C_6D_6 CD_3OD	33 26
 65b	120	C_6D_6	0.33
 67b	120	C_6D_6	9.7
 69	103 120	C_6D_6 C_6D_6	1.1 5.8

Scheme 32

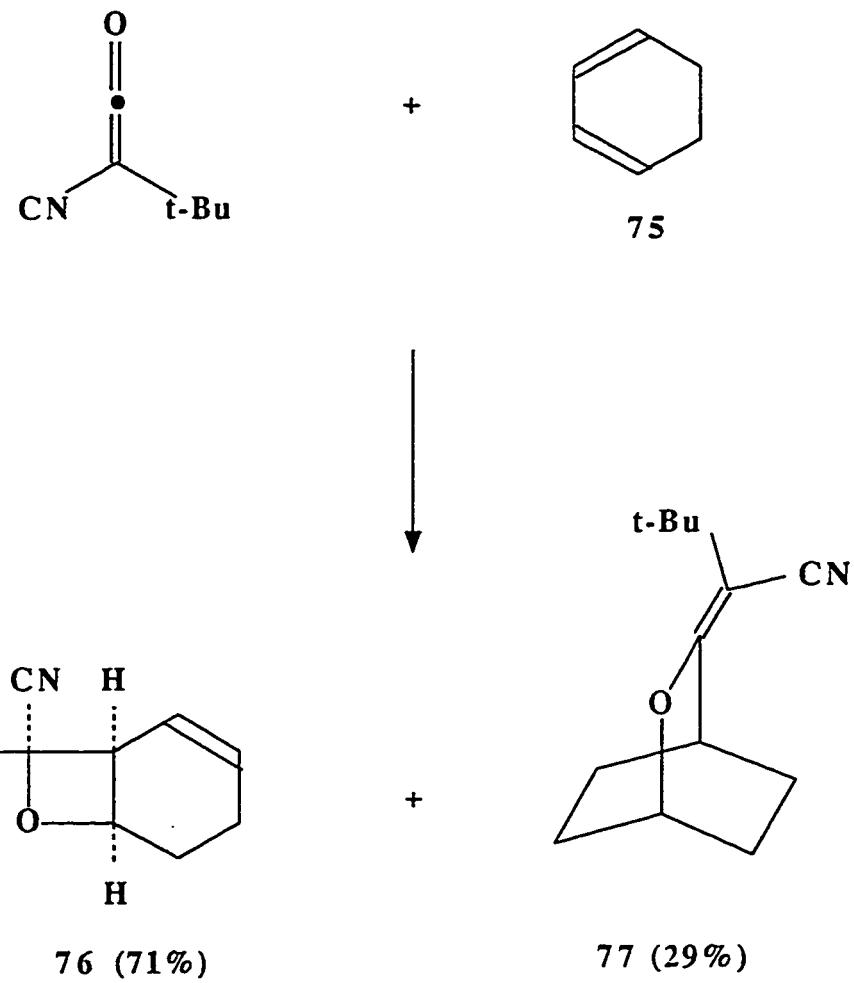


72



74 73

Scheme 33



concerted oxy-cope rearrangement or a stepwise process.

Similar cycloaddition of TBCK with 78 afforded a mixture of 79 and 80 (Scheme 34) in a ratio of 2.08 : 1 and 1.48 : 1.00 in benzene and acetonitrile respectively. This little solvent dependency suggests the concerted nature of the reaction.

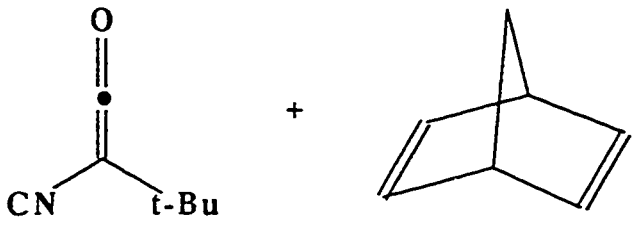
A zwitterionic mehcanism is most likely for the addition of TBCK to enol ether, vinyl acetate that gave the corresponding cyclobutanones 81 , 83 (3 : 1) and 82 , 84 (3 : 5) upon treatment with TBCK (scheme 35). Stereochemistry of the major isomer 81 , 83 is predicted to arise from a ($2\pi_s + 2\pi_a$) concerted process. However this theory was rejected since the product 86 (Scheme 36) obtained from 2-ethoxy propene could reasonably arise via zwitterionic intermediate 85 .

TBCK allene cycloaddition reactions have been suggested to occur via dipolar intermediate rather than by concerted process. Extensive studies have appeared concerning the cycloaddition of cyanoketenes to formimides, thioformimidates, and imines. The data accumulated so far establish these cycladditions to be dipolar in nature.

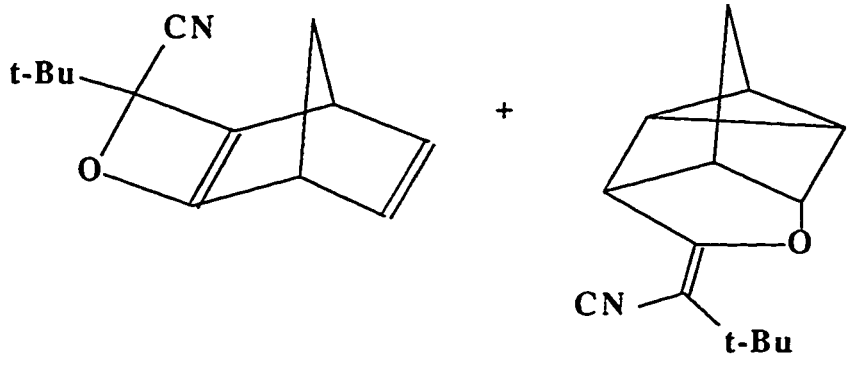
There are few reported cases[18,20] in which [2+2] cycloaddition of ketenes are suggested to proceed by non-concerted pathways (schemes 37, 38, and 39).

In these addition reactions, the intermediate zwitterions are stablized by resonance. However with normal alkenes, where resononance stablization is

Scheme 34

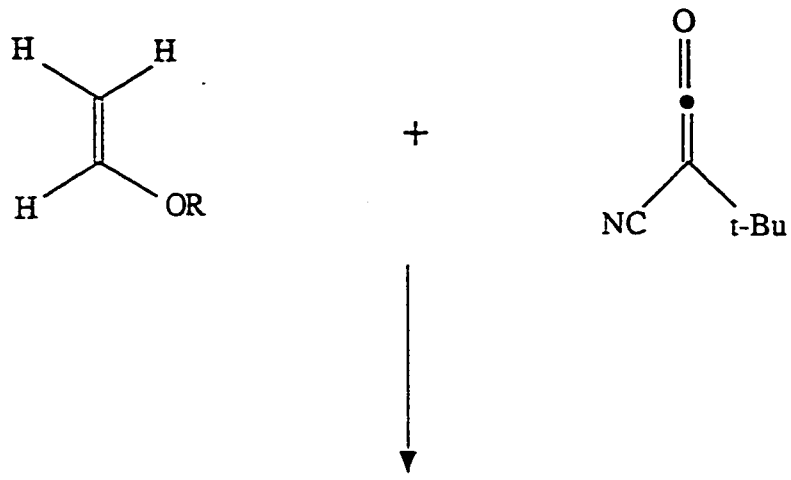


78



79 80

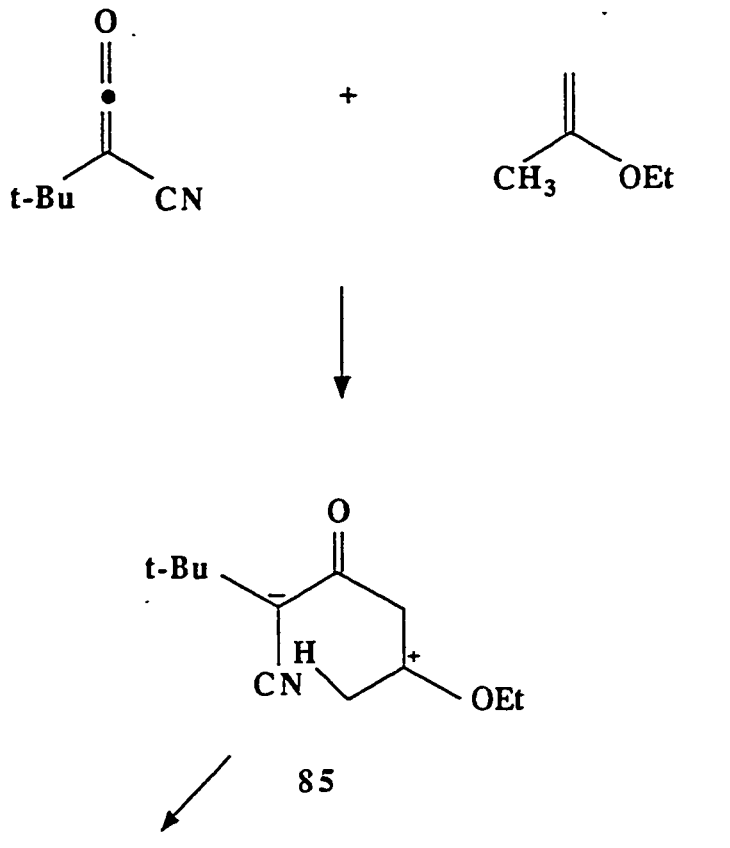
Scheme 35



81. (R= Et)
83. (R= COMe)

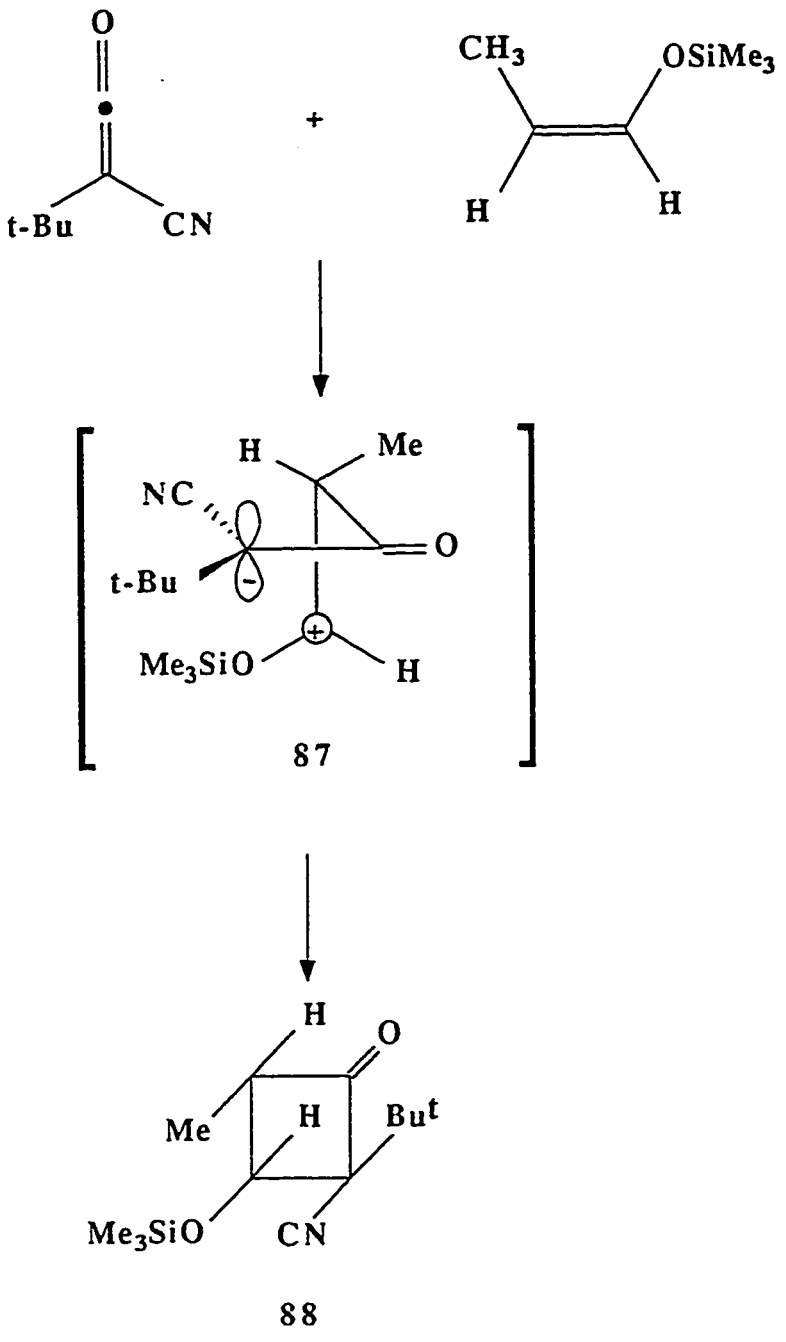
82. (R= Et)
84. (R= COMe)

Scheme 36

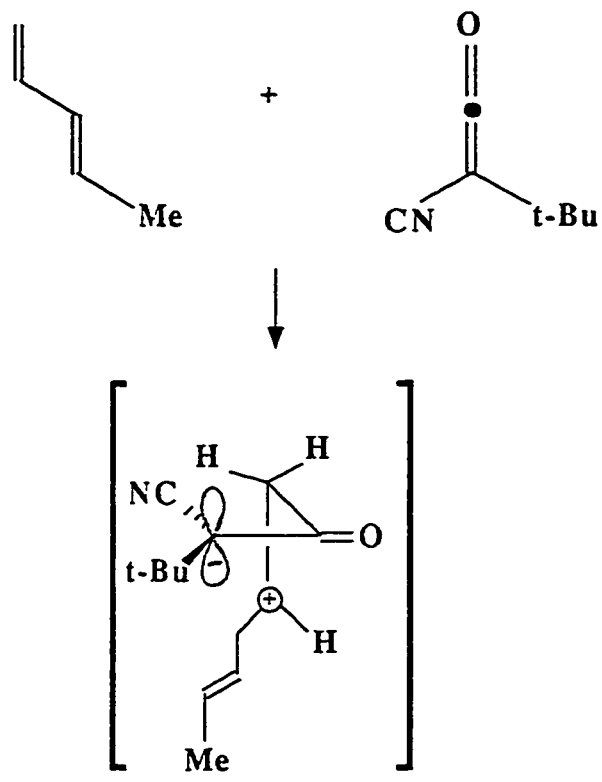


86

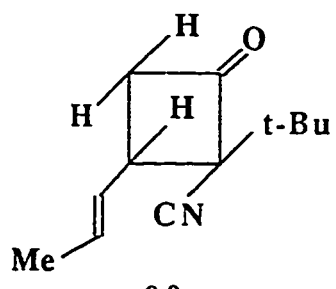
Scheme 37


O
t-Bu
CN
+
CH3
OSiMe3
H
H
H
Me
NC
O
t-Bu
Me3SiO
H
87
H
O
Me
H
But
Me3SiO
CN
88

Scheme 38

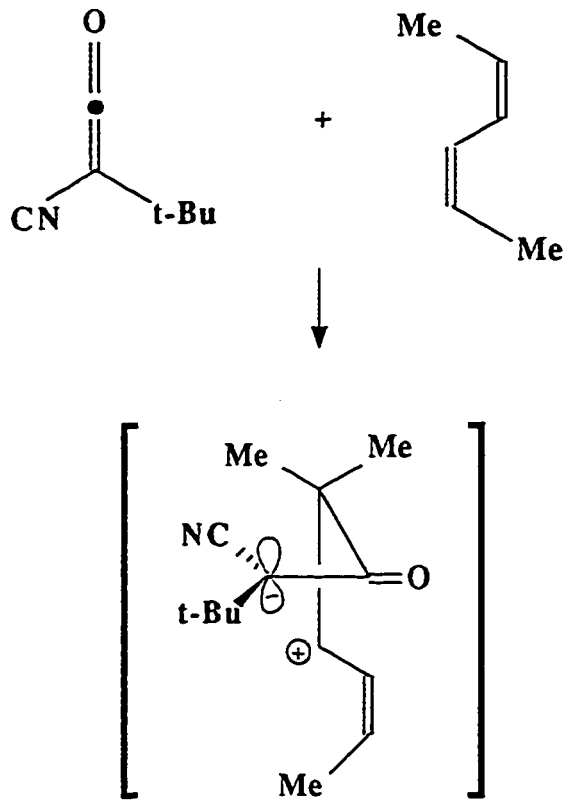


89

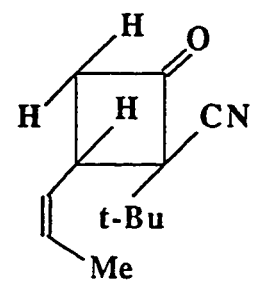


90

Scheme 39



91



92

not possible, the cycloaddition is thought to be concerted.

Cycloreversion of cyclobutanone to starting ketene and alkene or the [2+2] cycloaddition to cyclobutanone should follow the same pathway. In other words, if the addition reaction follows a stepwise mechanism the cycloreversion should be expected to follow the same pathway.

The results of our cycloreversion studies are included in table 10.

As can be seen, the rate of cycloreversion of 47 is more or less solvent independent. Thus it should be assumed to follow a concerted mechanism. The cycloreversion of 45 is very slow in comparison to that of 47. Cyclobutanone 47 is more crowded than 45 , because the former has two bulky groups at C-3. The crowding in 47 will be relieved in the transition state leading to the formation of ketene and alkene. Rate of cycloreversion of 65a in C_6D_6 and CD_3OD at 92° C was found to be approximately identical, thus ruling out the possibility of a zwitterionic intermediate. Styrene adduct 65a was found to break down 3.5 times faster in C_6D_6 at 92° C than C-3 disubstituted adduct 47. p-Methoxy styrene adduct 67b did not undergo cycloreversion at 92° C. However, at 120° C, the rate constant, k, for the decomposition of 67b was found to be $9.1 \times 10^{-5}\ s^{-1}$, which is approximately 30 times faster than that of the cycloreversion of styrene adduct 65b.

The rate constant for the cycloreversion of cyclohexene adduct 69 was found to be 1.1×10^{-5} and $5.8 \times 10^{-5}\ s^{-1}$, respectively, at 103° C , and 120° C in C_6D_6.

Rate constant values obtained for the cycloreversion of several cyclobutanones are of both theoretical and practical importance. Our study indeed provides some useful information regarding the stability of the ketene adducts.

In a dry NMR tube was taken 65a (80 mg), 64 (30 mg) and C_6D_6 (1.0 ml). The tube was then sealed and heated for 3.5 hours, at 92° C during which the NMR spectrum revealed very little isomerization of 65a to 65b (approximate ratio 90 : 10, respectively). However isomerization of kinetic adduct 65a to thermodynamic adduct 65b happened readily at 103° C. The above mixture of 65a and 65b (90 : 10) when heated at 103° C , after 6.15, 11.5, and 12.65 h, the ratio 65a and 65b found to be 53 : 47, 26 : 74 and 25 : 75, respectively. The ratio of the adducts 65a and 65b were determined by the integration of t-Butyl signlas that appeared at 0.78 and 0.90 respectively. It is known that cyano group deshields a cis, relative to a trans disposed adjacent proton in cyclobutanones. In C_6D_6 the C-3 H of 65a appeared at δ 3.89 as a triplet and C-4 H_A and H_B appeared at δ 3.16 and 2.62 as ABX pattern. However in the isomer 65b , the NMR signals for C-3 H moved more upfield as expected, and all the C-2 and the C-3 H appeared as a complex ABC pattern. Aromatic protons of 65a found to be shielded presumably due to steric crowding with cis oriented t-Butyl at C-2. Protons of 65a and 65b appeared at δ 6.98 and 7.15, respectively. We were unable to separate 65a and 65b by silica gel chromatography or by crystalization. However when a mixture of 65a and 65b (25 : 75) was heated to 92° C in the

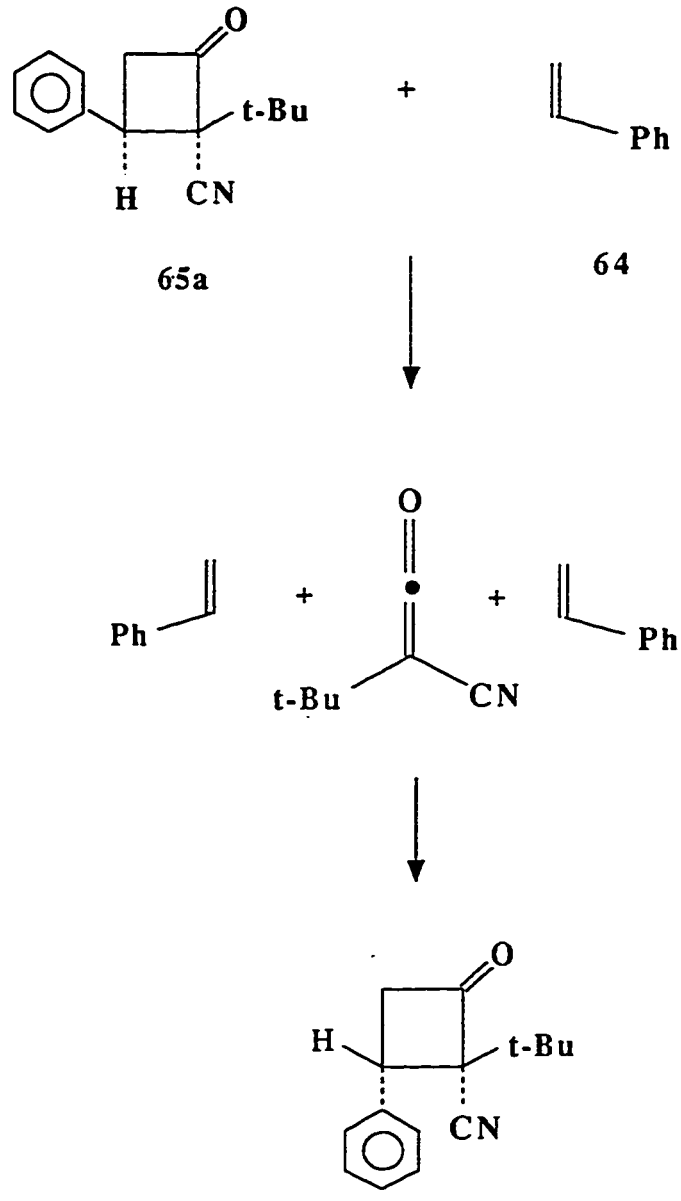
presence of trapping agent Methanol-d_4 for 6 hours, the contrathermodynamic isomer 65a underwent complete cycloreversion and the thermodynamic major isomer (65b) remained, as expected. unchanged. The half life for the cycloreversion of the cycloadduct 65a in C_6D_6 at 92° C was determined to be 35 minutes. But when the adduct 65a was heated at 92° C in the presence of styrene and absence of trapping agent (CD_3OD) for 3.5 h, only 10% isomeriztion to thermodynamic adduct happened. Thus cycloreversion was found to be much faster than isomerization. It is possible that the isomerization does not occur via a zwitterionic intermediate, rather the approach of styrene in two different orientations (Scheme 40) relative to TBCK affording the isomeric stable adduct 65b. Unlike styrene, the cycloaddition of p-methoxy styrene may involve zwitterionic intermediate. The prsence of p-methoxy group can stablize such intermediate by resonance. And kinetic adduct 67a can equilibrate to the thermodynamic adduct 67b (Scheme 41) easily via the zwitterionic intermediate.

3.3 Cycloaddition of TBCK to cyclic nitrones

Nitrones(Azomethin oxides) are well known 1,3-dipolar species, which readily undergoes cyloaddition reactions with a variety of unsaturated systems. However the corresponding reactions with ketenes is much less understood and examined to a limited extent[47].

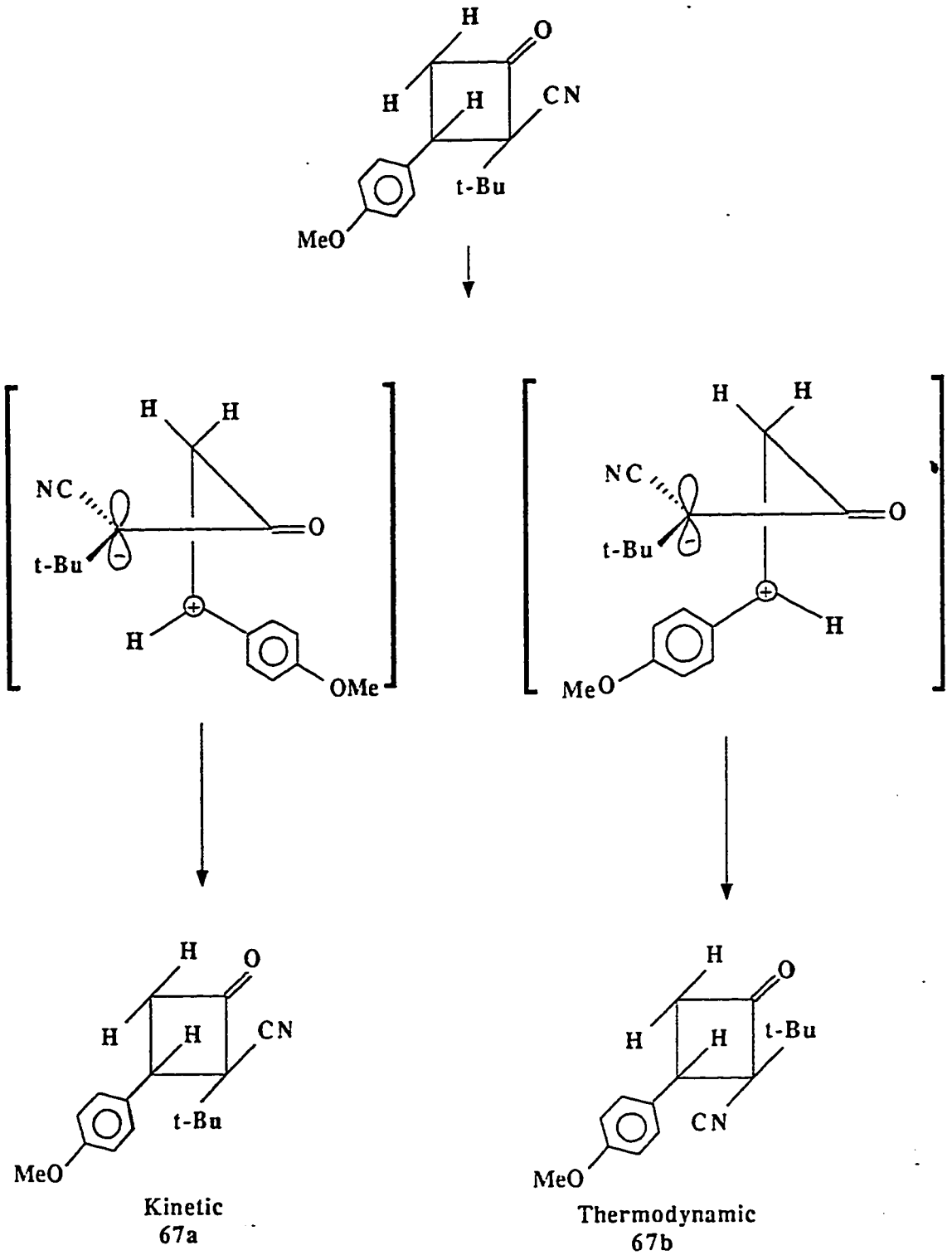
The cycloaddition of TBCK with th N-alkyl nitrones 93 afforded spiroisooxazolidine 94 (scheme 42).

Scheme 40



65b

Scheme 41



However, the corresponding addition reactions with N-aryl nitrone gave the spirooxazolidinone 96 rather 97, the expected cycloaddition product (Scheme 43).

It was suggested that the formation of 96 would arise from the decomposition of 97 to 98 and 99 which recombines.

The addition reactions of N-methyl nitrone with diphenyl ketene afforded a complex mixture of atleast five different products in low yield.

The reaction of N-phenylnitrone 100 (Scheme 44) with diphenyl ketene is reported to give an adduct wchich decomposes to CO_2 and another compound 104.

To our knowledge, no cycloaddition involving ketenes with nitrones having C-alkyl (instead of aryl) subtituent has been reported. It is our one of our objective to study the addition reactions of TBCK with cyclic nitrones.

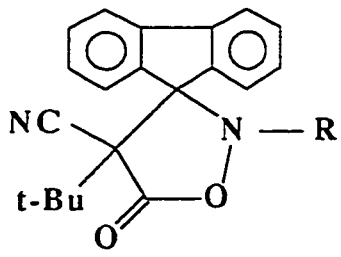
The cycloaddition of tert-butylcyanoketene to two different cyclic nitrones (Scheme 45) that contain β-H were investigated.

When a solution of 105 in toluene was added to TBCk. generated in toluene, at -30°,0°,20°, and 80° C in each case a complex mixture of products was obtained. The TLC experiment revealed several spots. The NMR spectrum did not give any useful information.

Similar addition of TBCK with 106 gave intractable mixture of products.

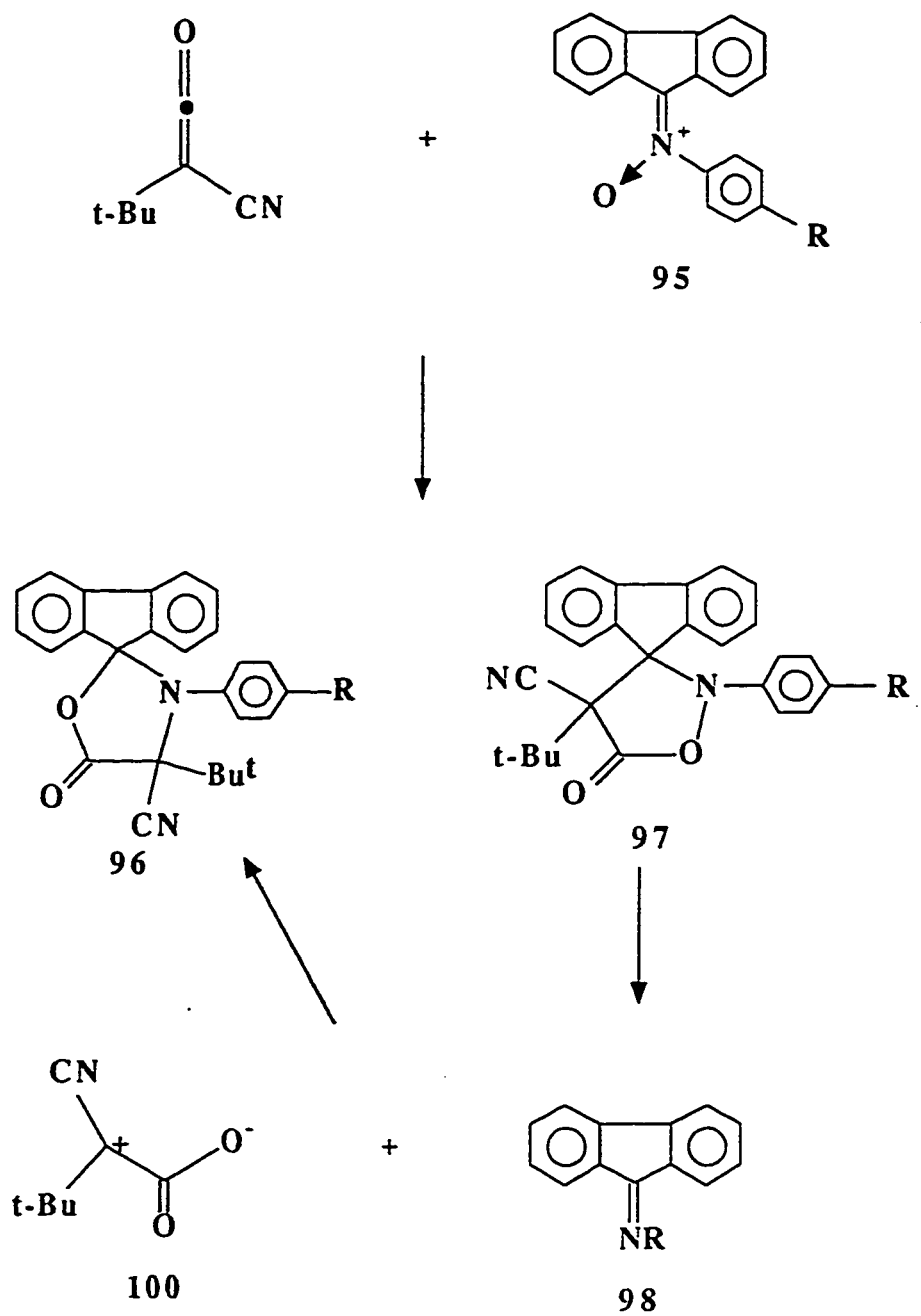
Scheme 42

93. R = Me, Et, CH_2Ar

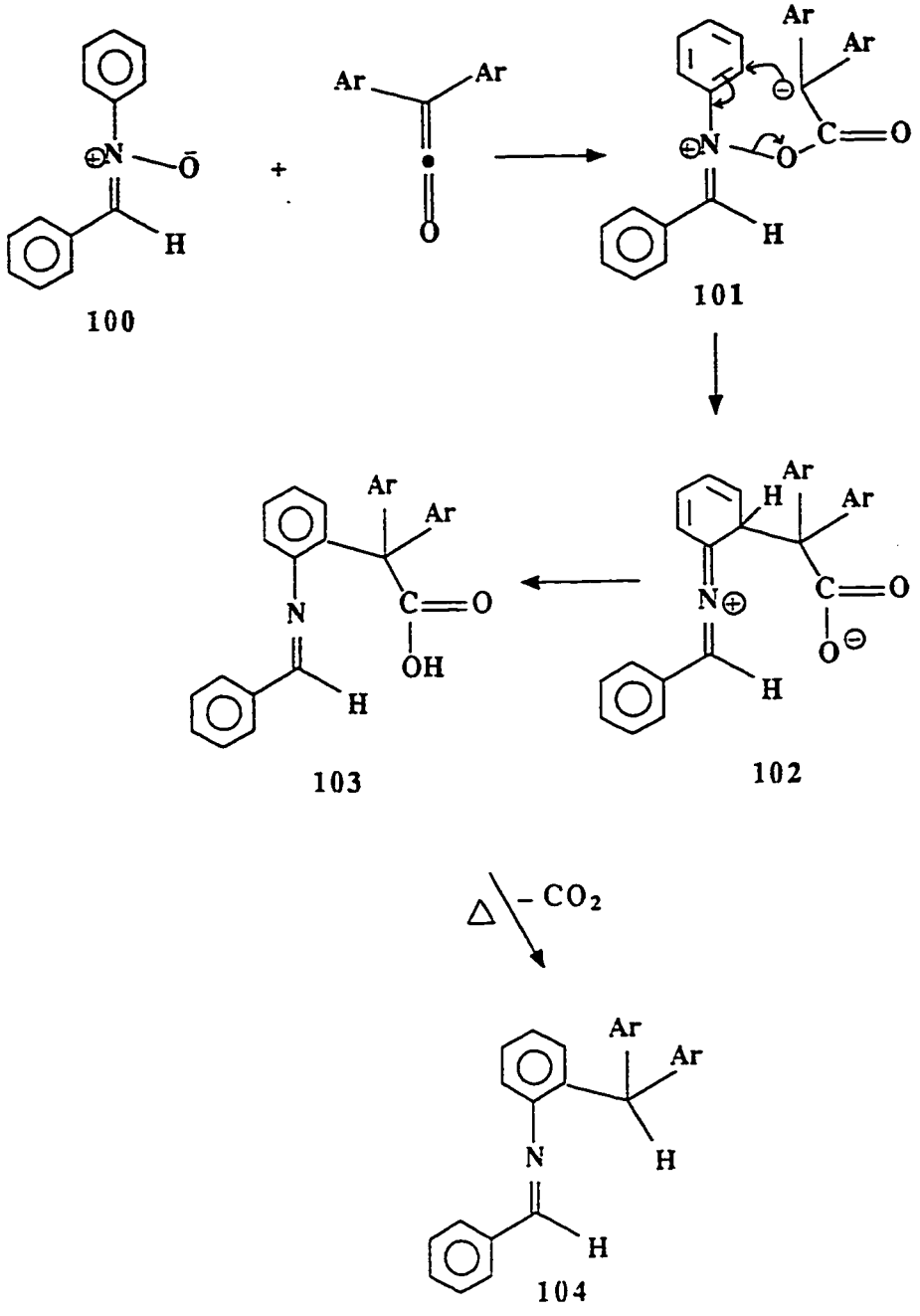


94. R = Me, Et, CH_2Ar

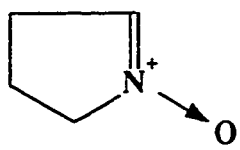
Scheme 43



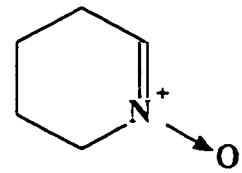
Scheme 44



Scheme 45



105



106

4. EXPERIMENTAL

4.1 General Comments

t-Butylcyanoketene was generated by the procedure described by Moor[1]. The diazaide compound (TBCK precursor) was dried under vacuum before thermolysis. The dry benzene/toluene/THF were prepared by pressing sodium wire in the solvent bottle and then further refluxing for 3-4 hours over CaH_2, finally distilling under dry argon ($NaOH-CaCl_2$) to give dry benzene/toluene/THF.

General procedure for the preparation of various silyl/benzyl ethers and alkenyl acetates used in this study is briefly described in the following pages. Pure starting silyl/benzyl ethers and alkenyl acetates were obtained by distillation under reduced pressure.

Infrared data were recorded on Nicolet DX-5. Solid samples were dried under vacuum before recording their spectra, whereas thin films of liquid and oily compounds on KBr/NaCl windows were used. All the IR absorptions of the compounds are expressed in wave numbers.

NMR spectra were recorded on a Brucker AC-80 nuclear magnetic spectrometer employing deuterated chloroform as solvent. In the thermal study of variety of cyclic compounds solvents like deuterated benzene (C_6D_6), deuterated methanol (CD_3OD) and deuterated dimethylsulfoxide ($DMSO-d_6$) were used. Chemical shifts of all the reactants and products are reported in parts per million , represented by δ , in chloroform. Tetramethylsilane (0.1%)

was used as internal standard, unless otherwise specified. The coupling constants are given in hertz (Hz). In reporting NMR data following order was maintained: chemical shifts (δ) , number of protons, multiplicity, and coupling constants.

Characteristic absorptions of NMR and all the IR absorptions of individual compounds are given in exerimental section.

Melting points of solid products were determined with an electrothermal capillary melting point apparatus.

Reaction products were separated on column packed with silica gel using different solvent ratios previously determined by thin layer chromatography.

4.2 Individual Procedures

4.2.1 Preparation of statarting materials

The ketene was prepared in nearly quantitative yield from its precursor 2,5-ditertiarybutyl-3,6-diazido-1,4-benzoquinone. The azide (3 mmol) was vacuum dried and dissolved in 50 ml of freshly distilled (CaH_2) benzene. The benzene solution was refluxed under anhydrous conditions (argon) for approximately an hour, the original deep orange color of the solution (azide) turned yellow (TBCK).

a. General procedure for preparationof t-butyldimethylsilyl alkenyl ether(s)

To a DMF (2X mL) solution of alkenol (X mmol) was added imimdazole (2X mmol) and t-butyldimethylsilylchloride (X mmol). The reaction mixture was stirred for 12 hours at room temperature. The mixture was then taken up in ether (100 ml), washed with distilled water ((4 × 100 ml) dried (Na_2So_4) and concentrated to give crude silyl ether which was then distilled.

b. General procedure for the preparation of benzyl alkenyl ether(s)

Sodium metal was added slowly (X mmol) to a stirring a solution of alkenol (X mmol). Some of the sodium metal was unreacted, unreacted metal was removed and benzylbromide (1/2 ×X mmol) added. Reaction was allowed to complete and extracted with ether (50 ml), washed the ether layer with distilled water (5 ×100 ml), dried (Na_2So_4) and concentrated to give crude benzyl alkenyl ether. Pure benzyl ether of the said alkenol was obtained

by distillation.

4.3 Cycloaddition of TBCK to silyl/benzyl alkenyl ethers/ alkenyl acetates

Cycloaddition of silyl/benzyl ethers and alkenyl acetates to TBCK was done under different temperatures.

a. Reflux Temperature Cycloadditions :

TBCK was generated under anhydrous (argon) conditions in a refluxing benzene. To a refluxing ketene solution was injected, with the help of syrenge, the desired amount of silyl benzyl ether/alkenyl acetates, and refluxing was continued for a desired amount of time,

b. Required Temperature Cvloadditions :

TBCK was generated under anhydrous (argon) condition in a refluxing benzene. After the generation of ketene the solution was brought to the required temperature and silyl/benzyl ether/alkenyl was injected with the help of a syrenge.

c. Room Temperature Cycloadditions:

TBCK was generated as mentioned above and cooled to room temperature, then silyl/benzyl ether/alkenyl acetate were a injected with the help of syrenge.

4.4 Characteristic properties of starting silyl/benzyl alkenyl ether(s)/ alkenyl acetate(s)

a. t-Butyldimethylsilyl-3-butenyl ether(42)

Colourless liquid; ν_{max} (neat) 3025(w), 2997(s) 1487(m), 1391(w), 1048(m) and 851(w) cm^{-1} ; δ_H ($CDCl_3$) 0.06(6H, s), .90(9H, s),2.27(2H, q, with fine splitting J 6.5 Hz). 3.66(2H, t, 6.5 Hz), 4.87-5.20(2H, m) and 5.52-6.37(1H, m).

b. t-Butyldimethylsilyl-4-pentenyl ether (44)

Colourless liquid; ν_{max} (neat) 3046(w), 2926(m) 2896(m), 2858(m), 2826(m) 1643(w), 1476(w), 1376(w), 1261(m), 1106(m), and 830(m) cm^{-1} ; δ_H ($CDCl_3$) 0.06(6H, s), .90(9H, s), 1.56-1.84(2H, m),2.14(2H, q, with fine splitting J 6.5 Hz), 3.66(2H, t, 6.5 Hz), 4.83-5.19(2H, m) and 5.56-6.57(1H, m).

c. t-Butyldimethylsilyl-3-methyl-3-butenyl ether (46)

Colourless liquid; ν_{max} (neat) 2932(s), 2832(s), 1647(w), 1389(w), 1269(m), and 1107(b) cm^{-1} ; δ_H ($CDCl_3$) 0.06(6H,s), 0.90(9H, s), 1.68(3H, app. s), 2.19(3H, t, J 7.0 Hz), 3.57(2H, t, J 7.0 Hz) and 4.67(2H, m).

d. Benzyl-3-methyl-3-butenyl ether (52)

Colourless liquid; ν_{max} (neat) 3040(m), 2940-2840(b), 1721(s), 1651(w), 1456(m), 1276(b), 1206(b),901(m), 751(m), 731(m) and 701(m) cm^{-1} ; δ_H

($CDCl_3$) 1.7(3H,s), 0.90(9H, app. s), 2.34(2H, t, J 7.0 Hz), 3.85(2H, t, J 7.0 Hz), 4.53(2H, s), 4.75(2H, m) and 7.35(5H,s).

e. 3-Methyl-3-butenyl acetate (56)

Colourless liquid; δ_H ($CDCl_3$) 1.783(H, app. s), 2.06(3H, s), 2.42(2H, app. t, J 7.0 Hz), 4.17(2H, t, J 7.0 Hz), 4.71(1H, m) and 4.78(1H, m).

f. Benzyl-2-methyl-2-propenyl ether (61)

Colourless liquid; ν_{max} (neat) 3039(w), 3005(w) 2900(w), 2840(w), 1721(m), 1457(m), 1389(w), 1265(w), -1199(b), 1034(w), 914((w), 749(m), and 709(m) cm^{-1} ; δ_H ($CDCl_3$) 1.75(3H, app. s), 3.83(2H, app. s), 4.30(2H, s), 4.99(1H, m), and 7.42(5H,s).

g. t-Butyldimethylsilyl-2-propynyl ether (70d)

Colourless liquid; ν_{max} (neat) 3820(m), 1935%(s) 2910(s), 2838(s), 2105(w) 1475(m), 1365(w), 1260(m), and 845(b) cm^{-1} ; δ_H ($CDCl_3$) 0.12(6H, s), 0.91(9H, s), 2.38(1H, t, J 2.2,Hz) and 4.30(2H, d, J 2.2 Hz).

h. Benzyl-2-propynyl ether (70f)

Colourless liquid; ν_{max} (neat) 3260(m), 3010(w) 2826(w), 2103(w), 1489(w), 1350(w)-1080(b), 1025(w) and 740(m) cm^{-1} ; δ_H ($CDCl_3$) 2.46(1H,t, 2.2 Hz), 4.18(2H, d, J 2.2 Hz), 4.60(2H, s) and 7.36(5H, s).

4.5 Individual Reactions

a. Cycloaddition of TBCK to t-butylydimethylsilyl-3-butenyl ether (42)

TBCK (6.0 mmol) was reacted with 42 in refluxing benzene for 12 h under argon. The reaction mixture was then concentrated and the residual liquid was purified by column chromatography over silica gel using 5:1 hexane/ether as eluent to give 43 as a colourless liquid in 70% (1.30 g) yield.

(E)-2-t-Butyl-2-cyano-3-(3-t-butyldimethylsiloxyethyl)cyclobutanone(43): colourless liquid; ν_{max} (neat) δ_H ; 0.06(6H, s), 0.90(9H, s), 1.23(9H, s), 1.85-2.25(2H, m), 2.85-3.50(3H, m) and 3.7.(2H, t, J 6.0 Hz).

b. Cycloadditionn of TBCK to t-butyldimethylsilyl -4-pentenyl ether (44)

The ketene (6 mmol) and t-butydimethylsilyl-4-pentenyl ether (44) was refluxed in benzene under argon for 20 hours. After removal of the solvent the NMR spectrum of the crude reaction mixture revealed the presence of a single isomer, we were unable to detect any minor isomer. Chromatographic purification over silica gel (10 : 1) as eluent afforded compound 45 as colourless crystal (0.900g, 61%),

(E)-2-t-Butyl-2-cyano-3-(3-t-butyldimethylsiloxypropyl)cyclobutanone(45): Colourless crystal; ν_{max} (KBr) 2848-2822(b), 2205(m), 1774(s), 1469(m), 1409(m), 1379(m), 1259(s), 1199(s) and 849 cm^{-1} ; δ_H ($CDCl_3$) 0.05(6H, s), 0.90(9H, s), 1.22(9H, s), 1.30-2.43(4H, m), 2.75-3.45(2H, m), and 3.67(2H, t, J 6.0 Hz).

c. Cycloaddition of TBCK to t-butyldimethylsilyl-3-mehtyl-3-butenyl ether (46)

To a solution of the TBCK (12 mmol) in benzene was injected the silyl ether (12 mmol) 46. The reaction mixture was refluxed under anhydrous conditions (argon) for 24 hrs. After removal of the solvent the crude yellow residue was chromatographed using hexane/ether (10 : 1) as the eluent to give the following fractions.

The first fraction eluted was compound 47 followed by a mixture of 47 and 48, then 48 and 49. Further elution afforded compound 49 and finally compound 50 in pure form. Thus we are able to isolate 47, 49, and 50, in pure form. However the NMR spectrum of 48, is deduced from the spectrum of the mixture containing 47 and 49. Detail analysis of NMR spectra and the mass of several fractions isolated revealed that the compounds 47, 48, 49, 50 were formed in a ratio of 40 : 33 : 19 : 8 respectively. The isolated yield of the products found to be 73% .

(E)-2-t-Butyl-2-cyano-3-methyl-3-(2-t-butyledimethylsiloxyethyl)cyclobutanone(47): R_f 0.63 (5 : 1 hexane/ether), colourless liquid; ν_{max} (neat) 2925(s), 2905(s), 2830(s) 2208(w), 1780(s), 1487(s), 1406(m), and 1137(m) cm^{-1} ; δ_H ($CDCl_3$) ; 0.07(6H, s), 0.90(9H, s), 1.25(9H, s), 1.51(3H, s), 2.20(2H, m), 2.78(1H, d, J 17.5 Hz), 3.38(1H, d, J 17.5 Hz), and 3.83(2H, dd, J 5.0, 7.0 Hz).

(Z)-2-t-Butyl-2-cyano-3-methyl-3-(2-t-butyledimehtylsiloxyethyl)cyclobutanone(48): R_f 0.60 (5 : 1 hexane/ether), colourless liquid; δ_H ($CDCl_3$) ; 0.07(6H, s), 0.90(9H, s), 1.28(9H, s), 1.54(3H, s), 2.20(2H, m), 2.75(1H, d, J 18.0 Hz),

3.41(1H, d, J 18 Hz) 3.80(2H, dd, J 5.0, 7.0 Hz), and 3.86(2H, d, J 18.0 Hz)

2-t-Butyl-7-t-butyldimethylsiloxy-5-methylene-3-oxo-heptanenitrile(49): R_f 0.54 (5 : 1 hexane/ether), colourless liquid; ν_{max} (neat) 2923(s), 2928(s), 2823(s), 1788(w), 1725(s), 1473(m), 1379(w), 1263(m), 1106(s) and 856(m) cm^{-1} ; δ_H ($CDCl_3$) 0.07(6H, s), 0.90(9H, s), 1.15(9H, s), 2.29(2H, t with fine splitting J 6.5 Hz), 3.38(3H, apparent singlet), 3.73(2H, t, J 6.5 Hz), 4.92(1H, bs) and 5.07(1H, m).

(E)-2-t-Butyl-7-t-butyldimethylsiloxy-5-methyl-3-oxo-hept-5-enenitrile(50): R_f 0.46 (5 : 1 hexane/ether), colourless liquid; ν_{max} (neat) 2940(s), 2925(s), 1724(m), 1444(w), 1389(w), 1259(m), 1114(w), 1074(m), and 847(m) cm^{-1} ; δ_H ($CDCl_3$) 0.07(6H, s), 0.90(9H, s), 1.13(9H, s), 1.65(3H, bs) 3.38(1H, s), and 4.22(2H, apparent d, J 6.5 Hz), and 5.44(1H, apparent t, J 6.5 Hz).

d. Cyloaddition of TBCK to benzyl -3-methyl-3-butenyl ether (52)

To a solution of the TBCK (6 mmol) in benzene was injected the benzyl ether (6 mmol). The reaction mixture was refluxed under argon for 4 hours and further continued at room temperature for 16 more hours. The solvent was removed and the yellow residue chromatographed using hexane/ether (5:1) as the eluent to give the following fraction containing 53 and 55 , followed by second fraction containing 53, 54, and 55. Finally the last fraction contained pure compound 54. The isolated yield of the product was 55%.

The above first fraction was further chromatographed using hexane/ether (5 : 1) as eluent to get a pure 53, we were unable to isolate 55 in pure form because of very close R_f values.

The analysis of several fractions isolated revealed the presence 53, 54, 55 in a ratio of 45 : 33 : 22 respectively.

(E)-2-t-Butyl-2-cyano-3-methyl-3-(2-benzyloxyethyl)cyclobutanone(53): R_f 0.35 (5 : 1 hexane/ether), colourless liquid; ν_{max} (neat) 2940(w), 2845(w), 2207(w) 1765(m), 1437(w), 1445(w),and 1112 (b) cm^{-1} δ_H ($CDCl_3$) 1.23(9H, s), 1.48(3H, s), 2.26(2H, app. q, J 6.3 Hz), 2.78(1H, d, J 17.5 Hz), 3.30(1H, d, J 17.5), 3.65(2H, dd, J 5.8,6.8 Hz), 4.48(2H, s), and 7.30(5H, m).

(Z)-2-t-Butyl-2-cyano-3-methyl-3-(2-benzyloxyethyl)cyclobutanone(54) ; R_f 0.21 (5 : 1 hexane/ether), colourless liquid; δ_H ($CDCl_3$) 1.26(9H, s), 1.48(3H, s), 2.12(2H, t, J 6.0 Hz), 2.73(1H, d, J 17.5 Hz), 3.30(1H, d, J 17.5), 3.65(2H, dd,J 5.8. 6.8 Hz), 4.48(2H, s), and 7.30(5H, m).

2-t-Butyl-7-benzyloxy-5-methylene-3-oxo-heptanenitrile(55): R_f 0.31 (5 : 1 hexane/ether), colourless liquid; The compound in a mixture of 53 and 55 displayed following identifiable signals δ_H ($CDCl_3$) 1.11(9H, s due to t-butyl group). The olefinic protons appeared at 4.42(1H, s), and 5.07(5H).

e. Cycloaddition of TBCK to 3-methyl-3-butenyl acetate (56)

Reaction of TBCK with 56 as before afforded a mixture of product 57, 58, 59. We were unable to separate the compounds individually, by

chromatography. The proton NMR data of individual compounds were deduced from the spectra of the mixtures rich in certain isomer. The integration of the t-Butyl proton indicated the presence of 57, 58, 59, in a ratio of 42 : 35 : 23, respectively. We could not detect the presence of the acyclic compound 60.

A total yield of 46% (700 mg) of the compound was isolated after purification. The IR spectrum of the mixture of 57, 58, 59, indicated the CN peak at 2247, and carbonyl of cyclic and acetyl at 1789, 1736 cm^{-1} respectively.

(E)-2-t-Butyl-2-cyano-3-methyl-3-(2-acetyloxyethyl)cyclobutanone(57): Colourless liquid; δ_H ($CDCl_3$) 1.23(9H, s), 1.50(3H, s), 2.05(3H, s), 2.30(2H, t, J 6.5 Hz), 2.80(1H, J 17.5 Hz), 3.25(1H, d, 17.5 Hz), and 4.23(2H, t, 6.5 Hz).

(Z)-2-t-Butyl-2-cyano-3-methyl-3-(2-acetyloxyethyl)cyclobutanone(58): Colourless liquid; δ_H ($CDCl_3$) 1.25(9H, s), 1.53(3H, s), 2.05(3H, s), 2.30(2H, t, J 6.5 Hz), 2.75(1H, d, J 17.5 Hz), 3.30(1H, d, 17.5 Hz), and 4.23(2H, t, 6.5 Hz).

2-t-Butyl-7-acetyloxy-5-methylene-3-oxo-heptanenitrile(59): Colourless liquid; δ_H ($CDCl_3$) 1.05(9H, s), 2.03(3H, s), 3.35(3H, two close space singlets), 2.40(2H, br. t, J 6.5 Hz), 4.19(2H, t, J 6.50 Hz), 4.98(1H, br. s), and 5.08(1H, br. s).

f. Cycloadditon of TBCK to benzyl-2-methyl-2-propenyl ether (61)

A solution of TBCK (6.0 mmol) and benzyl-2-methyl-2-propenyl ether (61) dry benzene was refluxed for 3 days. After removal of the solvent the crude adducts were purified by chromatography over silica gel using hexane/ether (5 : 1) as eluant to afford a nonseparable mixture of 62 and 63 as a colourless liquid (0.72, 42%) in the ratio of 55 : 45 as determined by the integration of methyl singlets. The NMR signal of 62 and 63 was deduced from the spectrum of their mixture.

(E)-2-t-Butyl-2-cyano-3-methyl-benzyloxymethyl cyclobutanone(62) ; δ_H ($CDCl_3$) 1.28(9H, s), 1.53(3H, s), 3.05(2H, AB, J 18 Hz), 3.67(2H, AB, J 12.00 Hz) 4.62(2H, AB, J 12.0 Hz). and 7.30(5H, s).

(Z)-2-t-Butyl-2-cyano-3-methyl-benzyloxymethyl cyclobutanone(63) δ_H ($CDCl_3$) 1.20(9H, s), 1.67(3H, s), 3.00(2H, s), 3.71(2H, AB. J 12 Hz) 4.65(2H, AB, J 12.0 Hz). and 7.30(5H, s).

g. Cycloaddition of TBCK to Styrene (64)

The cycloaddition of TBCK with 64 in refluxing benzene gave 65a (scheme 28) , in 80 % yield. The NMR spectra of 65a was found to be completely in agreement with the reported spectra[5-7].

(E)-2-t-Butyl-2-cyano-3-phenyl cyclobutanone(65a) ; δ_H ($CDCl_3$) 0.95(9H, s), 3.40(1H, dd, J 10.2, 18.0 Hz), 3.82(1H, dd, J 10.5, 18.0 Hz), 4.41(1H, t, J 10.5 Hz) and 7.20-7.26(5H, m).

(E)-2-t-Butyl-2-cyano-3-phenyl cyclobutanone(65a) ; δ_H ($C6_6D_6$) 0.80(9H, s), 2.65(1H, dd, J 10.2, 18.0 Hz), 3.15(1H, dd, J 10.5, 18.0 Hz), 3.90(1H, t, J 10.5 Hz) and 6.98(5H, app. s.)

(Z)-2-t-Butyl-2-cyano-3-phenyl cyclobutanone(65b) ; δ_H ($CDCl_3$) 1.20(9H, s), 3.30-4.00(3H, m) and 7.46(5H, m).

(Z)-2-t-Butyl-2-cyano-3-phenyl cyclobutanone(65b) ; δ_H (C_6D_6) 0.92(9H, s), 2.40-3.30(3H, m) and 7.12(5H, m)

h. Cycloaddition of TBCK to p-methoxy styrene (66)

Reaction of TBCK (6 mmol) with p-methoxystyrene (6 mmol) in refluxing benzene for 4 h resulted in the formation of 67a and 67b in a ratio of 40 : 60 as determined by the analysis of crude mixture. However we could isolate only 67b in pure form by silica gel column chromatography using hexane/ether (10 : 1) as eluant.

(Z)-2-t-Butyl-2-cyano-3-(p-methoxyphenyl)cylobutanone(67b); $\delta_H(C_6D_6)$ 1.20(9H, s), 3.14-4.12(3H, m) 3.80(3H, s) and 7.10(4H, AB, J 9.0 Hz)

i. Cycloaddition of TBCK to cyclohexene (68)

Reaction of TBCK with cyclohexene was done according to the procedure described by Moore[17]. TBCK (6 mmol) was generated in refluxing toluene and cyclohexene (6 mmol) was injected with the help of syrenge. Crude yellow coloured reaction product indicated the presence 69 by NMR. Pure 69 was obtained by silica gel chromatography using 10 : 1 (hexane/ether) as eluant.

The structure of 69 was confirmed with the similar one reported before.

7-Cyano-7-tert-butylbicyclo[4.2.0]octane-8-one(69) ; colourless solid, m.p 68-69° C ; ν_{max} (Nujol) 2235(CN), 1780(CO) cm^{-1} ; δ_H ($CDCl_3$) 1.23(9H, s), 1.2-2.3(8H, b), 2.9(1H, m) and 3.87(1H, m).

j. Cycloaddition of TBCK to variety of alkynes(70a-f)

The cycloaddition of TBCK and 70a (scheme 29) in refluxing benzene afforded 71a in good yield. The olefinic proton of 71a appeared at δ6.15. However the addition reaction of TBCK and 70b in benzene at various temperature and several trials afforded 71b in minor quantities. The olefinic proton of 69b appeared at δ 6.15 (J 1.8) as triplet. The corresponding reaction of TBCK with 66c at 20° C,50° C,80° C in benzene again gave only minute quantities of 71c. Repeated trails failed to yield appreciable quantities of the cycloadduct. The NMR spectrum of the crude reaction mixture displayed a 1H, triplet at δ 6.17(J 1.8 Hz). Similar reaction with 70d 70e and 70f at 20° C , 50° C , 80° C , and even in refluxing benzene for shorter or longer duration failed to give any identifiable cycloadduct.

Most probably the addition reactions with terminal aliphatic alkenes are either very slow at low temperatures or the highly strained adducts 71 formed at higher temperature may not survive the relatively harsh reaction conditions.

4.6 Thermal Studies of Various Cyclobutanones

a. Thermal Study of (E)-2-t-Butyl-2-cyano-3-methyl-3-(2-t-butyledimethylsiloxyethyl)cyclobutanone(47)

47 (60 mg), CD_3OD (30 mg) and C_6D_6 (1.0 ml) was taken in a NMR tube in N_2 atmosphere and the NMR tube was sealed. Thermal studies was now done at 92°C at various intervals of time and the course of the reaction was followed with the help of NMR.

The ratio of the alkene and the cyclic compound was obtained by integration of certain alkene and compound 47 signals. We have used the alkene and the C-4 proton of the cyclic compound.

Similarly thermal study of compound 47 was done in two more solvents (CD_3OD and DMSO- d_6) keeping thee amount of the compound, CD_3OD and the total volume of the solvent same.

b. Thermal Study of (E)-2-t-Butyl-2-cyano-3-(3-t-butyldimethylsiloxypropyl)cyclobutanone(45)

In an NMR tube was taken compound 45 (60 mg, 0.224 mmol), CD_3OD (30 mg, 0.83 mmol), and C_6D_6. (0.80 ml). The NMR tube was then sealed under N_2 and heated at 120°C. Table 4 indicates the result of thermal study of the above mentioned compound.

The ratio of 45 to 44 was determined from time to time by the integration

of CH_2O and the olefinic proton of 45 and 44, respectively, which were well separated.

c. Thermal Study of (E)-2-t-Butyl-2-cyano-3-phenyl cyclobutanone(65a)

In an NMR tube was taken 60 mgs (0.264 mmol), 30 mgs (0.83 mmol) of CD_3OD and C_6D_6. The total volume of the solution was 1.0 ml. The NMR tube was sealed in an inert N_2 atmosphere. The tube was then heated at constant temperature (92°C) oil bath and the course of reaction was followed with the help of NMR at various intervals of time. The integration of C-3 H of the adduct 65a and the olefinic protons of 64 were used to determine the concentration of 65a. Similarly the reaction was done by taking adduct 65a (60 mg) in CD_3OD as solvent and the reaction was followed at 92° C with the help of NMR as before.

d. Thermal study of (Z)-2-t-Butyl-2-cyano-3-phenyl cyclobutanone(65b)

65b (60 mg), CD_3OD (30 mg), and C_6D_6 (1.0 ml) was taken in an NMR tube in inert nitrogen atmosphere and the tube was sealed. The tube was then heated at 120° C and the course of the reaction followed with the help of NMR. Concentration of cyclic compound (65b) and the alkene (64) was determine from time to time by the integration of certain interested peaks.

e. Thermal study of (Z)-2-t-Butyl-2-cyano-3-(p-methoxyphenyl)cylobutanone(67b)

In an NMR tube was taken 80 mgs (0.321 mmol) 67b , 30 mgs (0.83 mmol) CD_3OD , and C_6D_6 making the total volume of the solution 1.00 ml.

The tube was sealed under N_2 atmosphere. The reaction was monitored at 103°C at various intervals of time. Concentration of 67b was determined by the integration of C-2 t-Bu group and C-3 H 67b.

f. Thermal Study of 7-cyano-7-tert-butylbicyclo[4.2.0]octane-8-one(69)

In an NMR tube 30 mgs (0.146 mmol) of the adduct 69, CD_3OD (20 mg) and C_6D_6 was taken making the total volume of the solution as 1.0 ml. The tube was then sealed under N_2.

Concentration of the adduct was determined at various intervals of time with the help of NMR by the integration of t-Bu of C-2 of the adduct 69 and the olefinic protons of the cyclohexene that appeared at δ 1.08 and 5.67 respectively.

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